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JOURNAL DE LA SOCIÉTÉ CANADIENNE DES ANESTHÉSISTES

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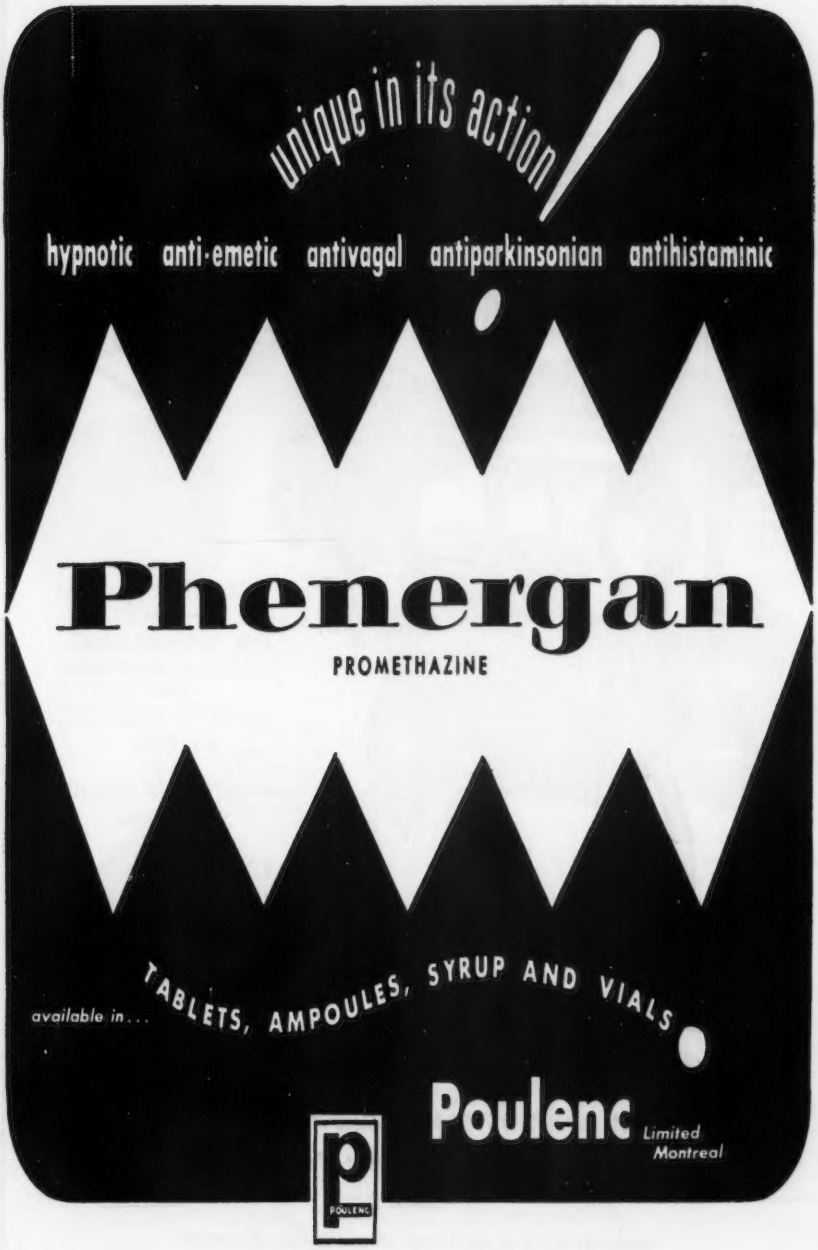
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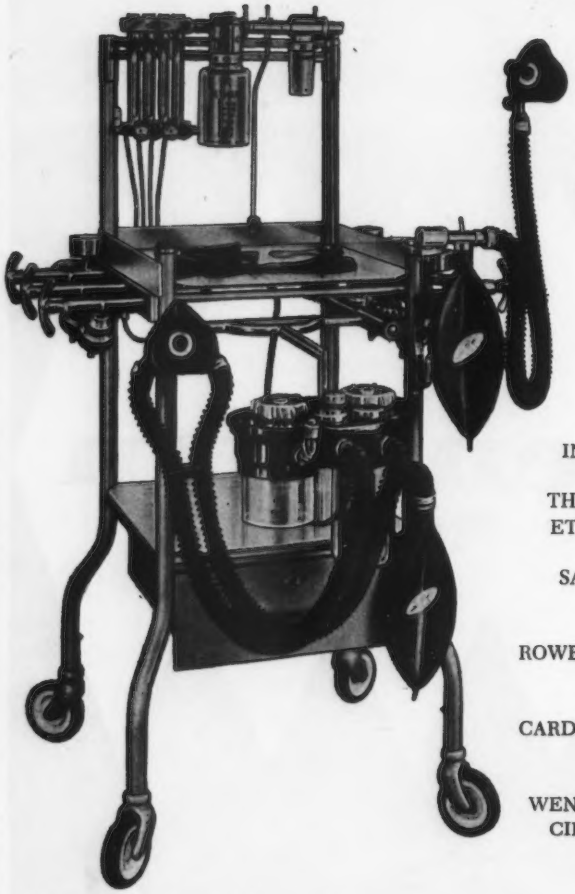

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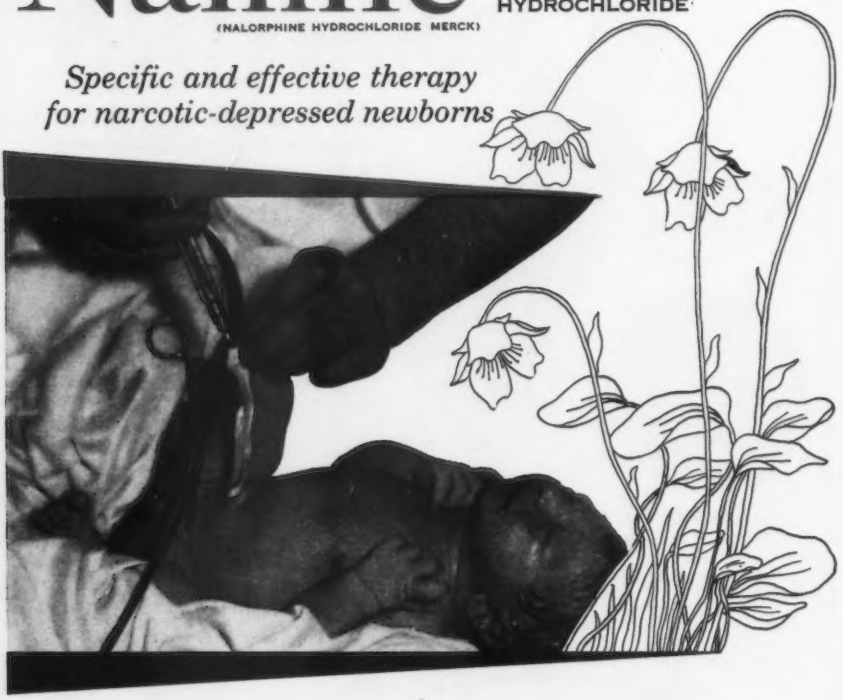

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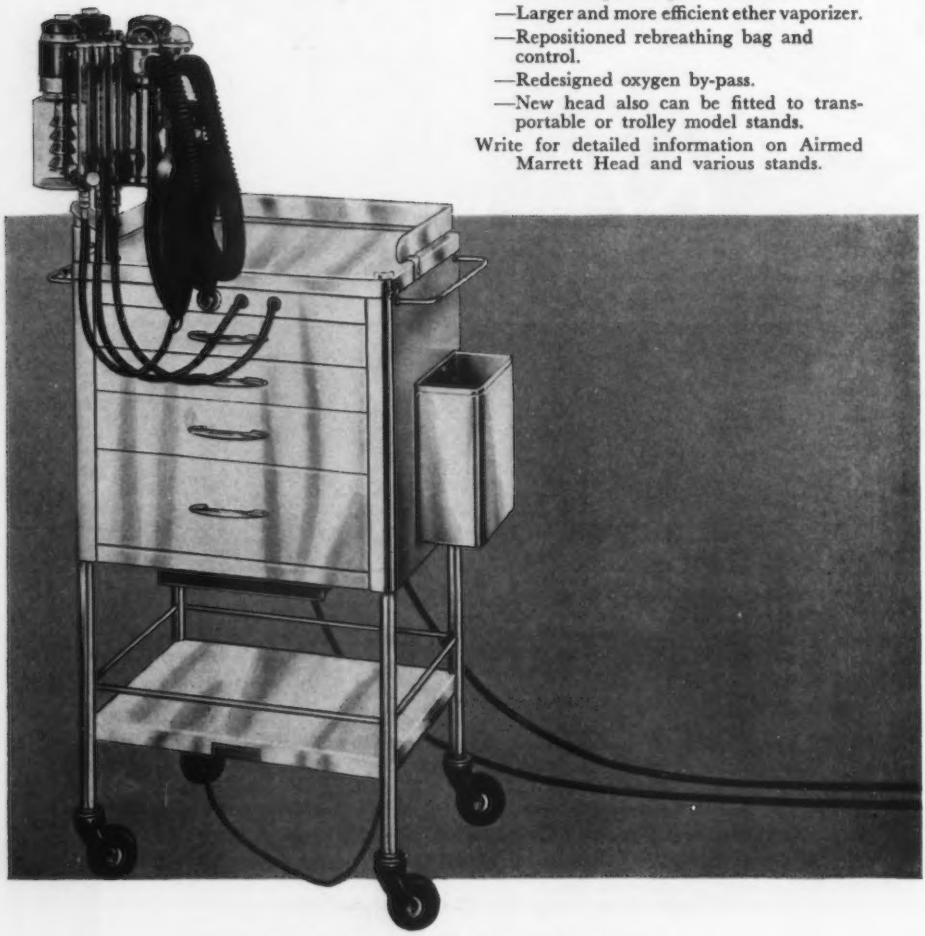

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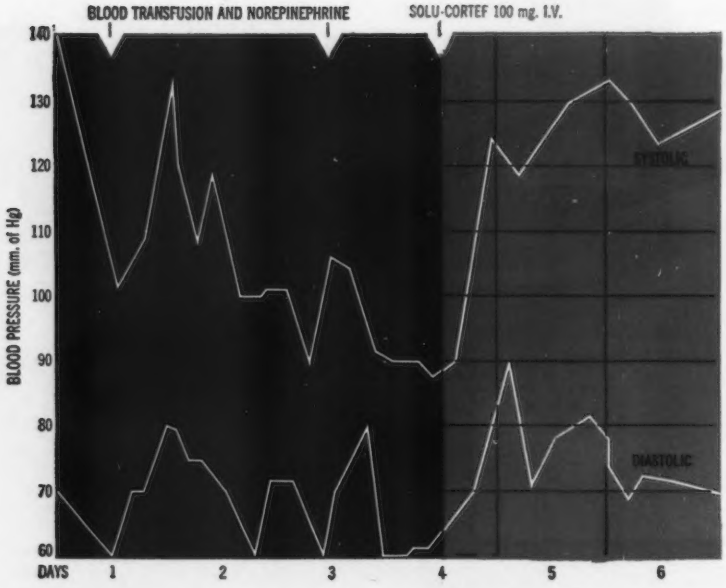

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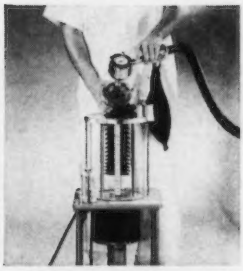

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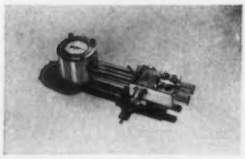

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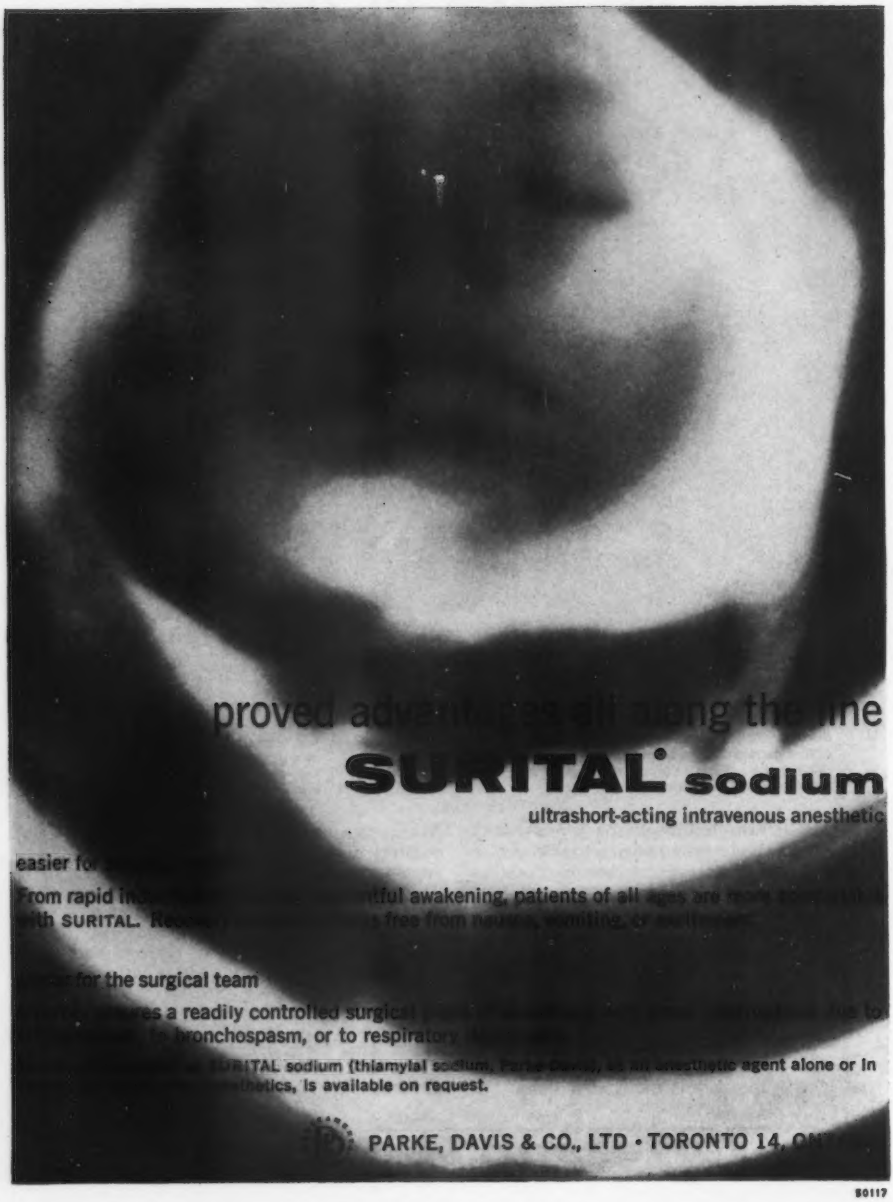
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EDITORIAL

Salute!

We take this opportunity to salute the *Canadian Journal of Surgery*, the brand-new and youngest member of the family of Canadian medical journals.

That this Journal will be a great success in its field is beyond doubt or conjecture, having as it does the services of Dr. Stanley Gilder as Editor, and the interest of a most distinguished Editorial Board under the Chairmanship of Dr. R. M. Janes. We offer our congratulations on the excellence of the first issue (October, 1957), and our best wishes for its future.

A New Home

We wish you a Happy New Year from our new home. True, we have only moved up the street a few doors, but we are pleased to think that our new arrangements will make it possible to deal more promptly with our correspondence with our readers, authors, advertisers and publishers, all of whom make the Journal.

The new address is:

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Salut!

Nous saisissons l'occasion de saluer le *Journal Canadien de Chirurgie*, le cadet et tout récent membre de la famille des journaux médicaux canadiens.

Il ne fait aucun doute que ce journal deviendra un grand succès étant donné qu'il a comme éditeur le Docteur Stanley Gilder et qu'il est sous la surveillance du comité de rédaction le plus distingué sous la présidence du Docteur R. M. Janes. Nos félicitations pour la qualité du premier numéro (octobre 1957) et nos meilleurs vœux pour l'avenir.

Un Nouveau Local

Nous vous présentons nos vœux de "Bonne Année" de notre nouveau local. C'est un fait, nous sommes déménagés à quelques portes seulement sur la même rue, mais il nous fait plaisir de penser que notre nouvelle installation nous permettra de faire plus rapidement notre correspondance avec nos lecteurs, nos auteurs, nos annonceurs et nos imprimeurs dont l'ensemble fait le Journal.

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THE ADRENAL CORTEX

Based on a Panel Discussion[1] with GORDON M. WYANT, F.F.A.R.C.S.,[2] *Moderator*; A. J. LONGMORE, F.R.C.P.(C),[3] and C. H. WEDER, F.R.C.S.(C),[4] *Members*

THE IMPORTANCE of the adrenal cortex in health and disease has been increasingly realized in recent years. The recognition, isolation and synthesis of some of its hormones have made possible the successful treatment of a number of disease states which previously had not been amenable to specific therapy. The relationship of certain diseases and disease syndromes to the adrenal cortex which had not been suspected before has now been clarified and this has allowed these conditions to be attacked on a rational and specific basis. Some of these diseases are of importance to the anaesthetist who must, therefore, have a working acquaintance with the physiology and pathology of the adrenal gland and the adrenal cortex in particular. It would, therefore, seem proper at this time to attempt a description of some of the known data on this subject, keeping in mind that it is a field which in many respects is as yet only partly understood, and that much of our present knowledge requires further elucidation or rectification. We shall limit this presentation in the main to a description of adrenal cortical hypofunction.

PHYSIOLOGY

The secretion of adrenal cortical hormone is regulated by the stimulation of ACTH produced by the anterior lobe of the pituitary gland. This in turn receives its stimulus from the hypothalamus. The resulting stimulation of the adrenal cortex produces the hydrocortisone which circulates in the blood and acts on all the tissues of the body (Fig. 1).

The production of this adrenal cortical hormone is regulated by two factors: (*a*) One is the amount of circulating corticoid. When this exceeds the amount required, the corticoid inhibits the pituitary from stimulating the adrenal cortex further. In conditions where the tissue need is great and where large amounts of circulating corticoid are used up, its level drops, thus inducing the pituitary to stimulate the adrenal cortex by producing more ACTH. In turn, if a patient is given cortisone as a medication, the level of circulating corticoid will be raised, inhibiting the pituitary; the production of ACTH will stop and consequently the adrenals will cease producing adrenal cortical hormone and become atrophic. In these cases there is potential danger if the exogenous cortisone is stopped, or if surgery is undertaken without realizing that the adrenal cortex is no longer active and that extrinsic support is required. (*b*) The

[1]Presented at the Annual Meeting of the Canadian Anaesthetists' Society, Saskatoon, Sask., June 24–26, 1957.

[2]Professor and Head, Department of Anaesthesia, University of Saskatchewan College of Medicine and University Hospital, Saskatoon, Sask.

[3]Chief, Section of Internal Medicine, Regina General Hospital, Regina, Sask.

[4]Clinical Associate, Department of Surgery, University of Saskatchewan, College of Medicine, Saskatoon, Sask.

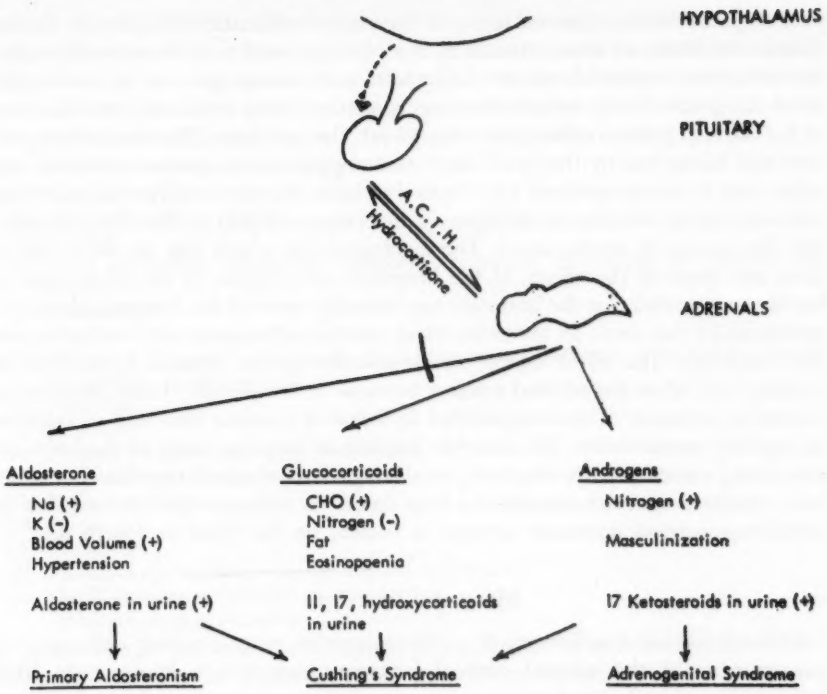

FIGURE 1

adrenal cortical output is also controlled by a central stimulus which acts on the hypothalamus. Variations in the intensity of this stimulus alter the amount of adrenal cortical hormones. In the morning a peak is reached and there is a lessening of output in the early evening and night. The production of cortisone by the adrenal cortex parallels that of cellular activity. In this connection it may be of interest to note that in Graves' disease, where cellular activity is high, the amount of adrenal cortical hormones necessary to maintain the body welfare is higher than normal. The role of the cortex is one of support rather than one of initiating action. The effectiveness of the hormone will depend on the state of the cells with regard to oxygenation and food supply. The gluco-corticoid portion of the adrenal cortex secretions has an anti-inflammatory effect, which may inhibit fibroblastic proliferation and thus retard healing.

Stress

It is well known that adrenalectomized animals or those with ineffective adrenal cortices withstand surgery and trauma poorly. This fact is corroborated by the

poor response to these stresses made by the patient with Addison's disease. Under normal conditions of stress, stimuli by the pituitary lead to an increased production of adrenal cortical hormone. In patients with severe burns or in irreversible shock the general body deterioration has sometimes been attributed to exhaustion of the adrenal cortex or its stimulating gland, the pituitary. This clinical impression was borne out by the good effect that supportive exogenous cortisone had when used to sustain patients who seemed to have deteriorated. We do know that adrenal cortical hormone of endogenous and exogenous nature does help to maintain the patient in severe stress. The mechanism by which this occurs is not so clear and some of the effects of the hormone even appear to be deleterious. It has been suggested that the hormone may detoxify some of the noxious substances produced by the stress on the cells; these noxious substances may be histamine-like chemicals. The effect on the cardiovascular system appears to be that of twining, and when the adrenal cortical hormone is completely absent, there is an "arteriolar asthenia." This is manifested by a loss of vascular tone and an increase in capillary permeability. The arteriole has lost its responsiveness to the ordinary circulating vasoconstrictor elements, producing a loss of circulating blood volume, and a diminution of the extracellular fluid space. In ordinary stress the amount of circulating cortical hormones returns to normal on the third or fourth day.

Medical Conditions

Adrenal cortical insufficiency is a comprehensive term denoting deficiency of one or more of the adrenal cortical hormones essential to homeostasis. This deficiency can be classified as:

1. *Primary*
   - (*a*) Adrenal destruction: tuberculous, 70–50%;[5] neoplastic, 5–10% (secondary); acute—overwhelming infection with toxaemia (Waterhouse-Friderichsen Syndrome.[6]
   - (*b*) Primary adrenal atrophy, 30–50% (becoming *more* common as T.B. becomes less).
2. *Secondary*
   - (*a*) Deficient ACTH from pituitary.
   - (*b*) Administration of steroids.

Adrenal cortical insufficiency may occur acutely and unexpectedly (*a*) when a

[5]

	Cases	*Due to T.B.*
Addison	11	5 (45%)
Guttman	566	(70%)
Rowntree and Snell	31	(84%)
Barker	28	25 (90%)
Coneybeare and Mills	29	22 (76%)
Wells	30	13 (43%)
Duffin	17	10 (59%)
Soffer *et al.*	33	21 (63%)

Snell (1934): "incidence of atrophy as a cause was increasing."

[6]Two hundred cases in literature to date: rare; common in children under five.

Martland (1944): 19 cases in 10,000 autopsies over 13 years—10 in children under 5, 9 in adults.

patient is subjected to anaesthesia and surgery, having previously been in a subclinical state of insufficiency; (*b*) in the course of severe and overwhelming infections; (*c*) during operation or postoperatively in those patients who have received steroids in the recent or distant past, when the steroids have suddenly been withdrawn. Steroid therapy has been used with varying success in a multitude of conditions. Among these are:

1. Adrenal atrophy
2. Addiction—drugs, alcohol
3. Asthma
4. Blood dyscrasias: leukaemias; haemolytic anaemias; thombopoenias, primary and secondary
5. Dermatitis
6. Burns
7. "Collagen diseases": rheumatic fever, rheumatic arthritis, polyarteritis, lupus, scleroderma, dermatomyositis
8. Hepatitis
9. Nephrosis
10. Mumps: orchitis, oophoritis, pancreatitis
11. Overwhelming bacteraemia
12. Pulmonary fibrosis
13. Sarcoidosis
14. Trichinosis
15. Intestinal dysfunction—"mal-absorption syndrome"
16. Shock (non-haemorrhagic)
17. Ophthalmological disorders

In obtaining a pre-anaesthetic history, it is advisable to question patients about suffering from any of these disorders, and to ask directly if they have been receiving "hormones." Many patients know the exact drug and dosage. We now know that the patients may not have regained full cortical function as much as one to two months after steroids have been discontinued. Periods of up to two years have been suggested by some authorities.

Lastly, a patient may have classical Addison's disease. This disease, although rare, is more common than realized. Soffer reports an incidence of 1 case per 4,500 hospital admissions. The classical picture is one of insidious onset and steady progression, of asthenia, loss of weight, anorexia with nausea and vomiting, and constipation–or abdominal cramps with diarrhoea. There is a "sun-tan" pigmentation of specific areas, exposed surfaces, flexor creases, buccal mucosa and genitalia, with anaemia, hypotension and susceptibility to infection. There is impotence and loss of libido in the male, amenorrhoea in the female, and irritability with personality changes.

Tests for Adrenal Function

1. *Cutler–Power–Wilder Test*: on constant intake of sodium, potassium and chlorine, there is excessive urine loss of chlorine.[7]

[7](1) .95 gm. NaCl and 4.1 gm. potassium per day, in measured diet; (2) after first day, and on morning of second day, 42 mg. of potassium citrate per pound of body weight, with water as desired; (3) after this ingested, fluid is limited to 40 cc. per kg. on second day; (4) on third day, fluid to 20 cc. per kg. until 11:00 A.M.; (5) urine is collected from 8:00 P.M. on second day until 8:00 A.M. of third, and from 8:00 A.M. until noon of third day. This is analysed for quantity of chloride: normal is 17–141 mg. % (average–54); Addison, 229–356 mg. % (average–290).

2. *Robinson–Kepler–Power Water Test*: 1500 ml. water is drunk in 45 minutes. The normal patient excretes 800 ml. or more urine in 5 hours; the "Addison" patient excretes less than 800 ml.

3. *Determination of* (*a*) *17-keto-steroids*, (*b*) *11-oxy-steroids*, in urine[8] before and after stimulation by ACTH–25–30 units intramuscularly.

4. *Glucose Tolerance Test*: orally or intravenously.

5. *Thorn Test*: after 20–25 mg. ACTH is injected intramuscularly, the eosinophil count falls after 4 hours by 50 per cent or over.

Treatment of Adrenal Cortical Insufficiency

For clinical purposes, we have in treatment:

1. *Salt*: Ordinary diet; 6–8 gm. per day; may need to add another 1–2 gm.

2. *Desoxycorticosterone acetate*: (*a*) In sesame oil for intramuscular use; (*b*) as aqueous percorten glucoside for intravenous use; (*c*) trimethylacetate for intramuscular use (an ester in micro-crystalline suspension–lasts 4–6 weeks); (*d*) pellets for implantation; (*e*) DOCA in propylene glycol–sublingual.

3. *Cortisone and hydrocortisone*: cortisone, 25–50 mg. per day; hydrocortisone, 20–40 mg. per day.

4. *Alpha-9-fluorohydrocortisone*: .25–.5 mg. per day.

5. *Aldosterone*: .1 mg. (orally or intramuscularly) 2–3 per day.

6. *Whole adrenal cortical extract*: expensive, uncomfortable.

7. *Combinations* of above.

8. *Best regimen* seems to be (*a*) full diet and extra salt if necessary; (*b*) daily oral dose of one–commonest 3, 4 or 5 above; (*c*) one of DOCA compounds intramuscular every 1–6 weeks as needed; (*d*) patients should carry a card with name, address, diagnosis and above dosages in detail.

Complications of Treatment

1. Congestive heart failure.
2. Myocardial infarction.
3. Hypertension.
4. Spread of infection–unrecognized.

[8]Determination of (*a*) 17-keto-steroids in urine–normal varies according to age and sex, with a wide range in any one group:

	Mg./24 hr.
To age 7	1.3
7–12	4.0
12–15	8.2
Adult male	15.0
Adult female	10.2

Alpha comprise 85–90%; beta comprise 15–10%; beta fraction markedly increased in cortical carcinoma.

Determination of (*b*) 11-oxy-steroids in urine–normal range varies in different laboratories and with method used: (1) colorimetric (Talbot)–.12–.34 mg./24 hr.; (2) periodic oxidation and measurement of formaldehyde liberated: Daughaday–1.0–2.0 mg./24 hr.; Soffer–0.5–2.0 mg./24 hr.

5. Perforation of viscus—pre-existing ulcer or spontaneous.
6. Gastro-intestinal haemorrhage.
7. Psychosis.
8. Spontaneous fracture.
9. Adrenal cortical atrophy (does not occur following ACTH therapy).
10. Hyperglycaemia (aggravated by pre-existing diabetes mellitus).

Relative Contraindications to Adrenal Cortical Therapy

1. Active tuberculosis: pulmonary, osseous, renal (now all right with antibiotic coverage—streptomycin+PAS, or streptomycin+INH).
2. Peptic ulcer: ulcer régime—diet, alkali, anti-spasmodic, etc.
3. Chronic renal disease.
4. Congestive heart failure.
5. Myasthenia gravis.
6. Psychosis.
7. Hypertension.
8. Diabetes mellitus.
9. Osteoporosis.
10. "Emotional lability."
11. Hirsutism in the female.
12. Surgery.

Surgery of the Adrenal Gland

The surgeon's interest in the adrenal cortex is twofold. First, he is interested in those diseases which attack the adrenal glands or those conditions in which the removal of the adrenal glands may affect other diseases of the body such as secondary carcinoma of the breast. Secondly, he is interested in the normal role of the adrenal cortex in such conditions as shock, peptic ulceration, the healing of wounds, the use of homografts and the effect on the inflammatory process.

There are four diseases or conditions in which surgery is used to remove one or both adrenals (1) secondary carcinoma of the breast; (2) unilateral or bilateral non-endocrine tumours of the adrenals; (3) tumours of adjacent organs such as the kidney; (4) abnormal conditions of adrenal function which are manifested by a hypersecretion of the adrenal cortical hormone.

In the first three groups it is necessary to supplement the normal adrenal cortical hormone by substitution therapy. In carcinoma of the breast, it is particularly advisable to do this, even if the adrenals are being removed in two stages, because it has been found that in at least a third of the cases, after one gland has been removed, the remaining adrenal has been afflicted with secondary carcinoma and thus its function is impaired. With the removal of non-endocrine tumours or adjacent tumours involving the adrenal, supplemental therapy is wise as a precautionary measure. This is especially true in phaeochromocytoma where the tumour is often bilateral and malignant. While the cortex is not the site of the tumour, and is not by itself hypersecreting, it invariably has to be removed to eradicate the medullary tumour.

Hyperfunctioning conditions of the adrenals. The basis of this hypersecretion may be secondary to some other stimulation, presumably that of the pituitary, or it may be due to an independently functioning tumour. Adrenal cortical over-activity may manifest itself in a variety of clinical syndromes.

The first and most recently discovered is that of *primary aldosteronism* in which there is a retention of serum sodium and water, a depression of potassium with secondary hypertension. In advanced cases, alkalosis, periodic paralysis, tetany and polyuria are apparent. This condition is almost invariably due to tumour. Temporary and decreasing corticoid cover is wise after its removal to prevent a too rapid return to a normal endocrine pattern. The dosage here however would be given intravenously, as needed, rather than as a heavy intramuscular medication which is not too readily controllable.

The second condition is *Cushing's syndrome* in which there is excess of gluco-corticoids, the androgenic corticoids, as well as the electrolyte effect in variable proportion. The anaesthetist has to contend with hypertension, the bullneck obesity with its airway difficulties as well as with the problem of hormone management during operation. If the disease is due to a unilateral tumour, the blood serum has been flooded with an excess of gluco-corticoids which has acted, through the pituitary, to depress the other adrenal. On removal of the adrenal tumour the patient is then left in an "Addisonian" condition and must be supported with intravenous corticoid therapy. If a preoperative diagnosis is made, intramuscular corticoid support on the two days previous to operation would be advisable to form a cushion for the intravenous supplement. When Cushing's disease is due to hyperplasia, supplemental therapy is necessary if both adrenals are completely removed or if a subtotal adrenalectomy is done because of the difficulty in assessing both the amount of adrenal which remains behind and the efficiency with which this remnant may function.

The third condition of hyperfunction of the adrenal cortex for which surgery is sometimes done is the *adreno-genital* syndrome which, like Cushing's syndrome, may be due either to tumour or to secondary hyperfunction. In this condition the problem is quite similar to that in Cushing's disease.

Recently workers have been doing total adrenalectomies for certain types of malignant hypertension and the problem here is simply one of supplemental therapy.

Anaesthetic Considerations

Reference has been made in previous paragraphs to the importance of determining from the patient's history whether cortical steroids have been administered previously and, if they have, of reinstituting cortisone therapy preoperatively. Prophylactic administration of cortisone is also required for all operations on the adrenals or in cases where removal of one or both glands is contemplated. Patients who are actually on steroid therapy should have the dosage increased before operation.

The aforementioned indications for adrenal steroid therapy are quite straightforward. The only questions are how much hormone should be given pre-

operatively, and how long after cessation of therapy it is safe to dispense with prophylactic medication, when performing such an operation.

A dosage of 100 to 150 mg. of cortisone per day orally for two or three days preceding operation and a further intramuscular dose on the morning of operation would seem adequate for most patients except those who are on steroid therapy, for whom it is just a matter of increasing the maintenance dose. Hydrocortisone, prednisone or prednisolone may be used in place of cortisone.

The question as to how long after previous therapy it is safe to operate without resuming hormone substitution is still controversial. Some authorities insist that in some patients there is residual latent adrenal insufficiency for many years. Today, with rapid acting intravenous steroid preparations available, this question is more academic than real, since, if such impairment of adrenal function persists, and becomes clinically manifest in the course of operation, immediate administration of intravenous aqueous hydrocortone will avoid difficulties. It would therefore seem reasonable to set an arbitrary limit of two years, being fully cognizant that in an occasional case this may be too short a period.

Latent Adrenal Insufficiency

This condition is not infrequently encountered in chronically ill patients, often suffering from advanced malignancies, or other chronic debilitating conditions, who are undergoing prolonged or radical operations. These individuals have usually lost weight, have poor skin turgor, look haggard and may be assumed to have a restricted circulating blood volume. The clinical picture consists essentially of progressive hypotension accompanied or not by increasing tachycardia, pallor, perspiration, and possibly air hunger, although these symptoms are neither as constant nor as pronounced as in oligaemic shock. The syndrome commonly appears in or after the second hour of operation and not infrequently supervenes after completion of the surgical procedure. It does not respond to vigorous blood and fluid replacement or to the administration of potent vasopressors which are ineffective or have a fleeting effect only, even if administered as an intravenous infusion. The condition is not reflex in origin and does not respond to the administration of atropine in large doses. If untreated the condition is progressive and the patient may die despite heroic measures. Experience has shown that these patients do respond, however, to prompt treatment with intravenous hydrocortisone. With experience, one is soon able to anticipate many of these cases; it is then wise to start steroid therapy before difficulties arise. Hydrocortisone 100 mg. is administered intravenously every four hours during operation, or if hypotension is already present it may be given more frequently until an adequate blood pressure has been restored. Administration is reduced to three times daily on the first postoperative day, twice daily on the second postoperative day, and one last injection is given on the following day, if the patient is able to maintain adequate homeostasis on this regimen of weaning. If hypotension recurs, the daily dose is increased again. Massive but short-lasting medication of this type does not seem to influence adrenal activity to the point where the patient becomes permanently dependent upon substitution therapy. Nor, in our experience, does

it seem to interfere with wound healing. We have observed no evidence of electrolyte imbalance, but we are routinely opposed to the administration of sodium chloride solutions for the first two postoperative days if there was no pre-existing electrolyte imbalance, and hence the question of sodium retention does not arise.

It is of course true that hydrocortisone in itself has no vasopressor activity; at least we have failed to show any such activity in normotensive human beings. It has been postulated that cortisone conditions the metarterioles to the action of endogenous epinephrine and there is some good experimental evidence to support this view. However, it seems that at least in normal individuals, no correlation can be established between the action of hydrocortisone and epinephrine; in experiments conducted on human volunteers we have been unable to establish any such correlation. These volunteers were given one millilitre of norepinephrine 0.0002 per cent intravenously, and pulse and blood pressure responses were observed and recorded. There was usually an immediate peak pressure response which gradually returned to pre-experiment levels in about thirty minutes. Several hours later, hydrocortisone 100 mg. was administered intravenously followed by hourly eosinophil counts. When the eosinophil count had fallen to approximately 50 per cent of the pre-experiment level, the same amount of norepinephrine was again administered and blood pressure and pulse responses again noted. In no case was a subsequent hypertension greater or more prolonged than in the control experiment. This seemed to indicate that in healthy and normotensive individuals at least, a peak effect of vasoconstriction is obtained by norepinephrine alone and is not potentiated by the previous administration of cortical steroids.

Sandberg found that general anaesthesia was followed by an increase in steroid concentration in eight of twelve patients. In twenty-two patients, eleven of them with malignant disease, Virtue has recently reported that dihydroxycorticosteroids increased on the average from 11 gamma per cent to 25 gamma per cent after one hour, and 34 gamma per cent after three hours of operation. There was no significant difference for patients with non-malignant and malignant disease. However, this observation does not materially assist the argument that some cases of hypotension may be due to adreno-cortical insufficiency since (*a*) steroid blood levels do not tell the whole tale of adrenal function; and (*b*) more important still, none of Virtue's malignant cases showed shock. A very large series of cases would be necessary in order to include a sufficient number of "adrenal shock" to be able to compare them with those who do not exhibit this phenomenon. This would be an undertaking of considerable magnitude.

It would seem reasonable to formulate a concept that in severely and chronically ill patients one deals with a state of borderline adrenal function. Thus, adrenal function is adequate in these individuals to take care of the daily needs and stresses which in these particular patients are not very great as a rule. When great stress is imposed, their adrenal function is inadequate to deal with it and relative adrenal insufficiency develops. As soon as, after a few days, the peak stress has disappeared, adrenal function is again adequate to cope with an uncomplicated normal convalescence. It has been found experimentally in adrena-

lectimized animals that in the phase of severe stress the substitution therapy which was adequate for these animals under normal conditions becomes inadequate and this has been termed "relative cortisone deficiency." It seems eminently reasonable that a similar state of affairs could obtain in some types of patient. Burstein has recently described a short bedside test to determine adrenal function by estimating the sodium concentration in plasma and urine by means of a flame photometer. In adrenal cortical insufficiency there is significant reduction in the serum sodium concentration (less than 130 mEq./litre) and a higher excretion of sodium in the urine (more than 100 mEq./litre). It has been found that during general anaesthesia, and in the absence of an excitement stage, there is an increase of 17-hydroxycorticosteroids in the plasma with a normal eosinophil count. This combination is difficult to explain unless one surmises that the disturbances of liver and kidney function during general anaesthesia interfere with the usual conjugation and excretion of the adreno-cortical steroids, resulting in a disturbance of the balance between their secretion and utilization on the one hand, and destruction and excretion on the other.

Premedicant drugs seem to have a certain influence on adreno-cortical function, mainly through the pituitary-adrenal axis. Thus morphine causes diminution of secretion of ACTH by the pituitary resulting in depressed adreno-cortical function. The same effect has been shown for pentobarbital. Administration of therapeutic doses of pentobarbital produces a significant fall in the free serum corticoid level from twelve to six micrograms. However, subsequent intravenous administration of ACTH results in the usual rise of corticoids which seems to point to a depression of the formation of ACTH, possibly by means of an altered hypothalmic threshold. Psychic stress from apprehension and anxiety in the preoperative period is also important. In healthy subjects, it has been shown that urinary secretion of 17-hydroxycorticosteroids rises from a mean level of 1–4 micrograms per minute to 5.6–8.3 micrograms when feelings of apprehension, anger or excitement are present. On the other hand, the over-all effect of anaesthesia on adreno-cortical function would seem to be a blockade of traumatic stimuli. A number of clinical reports have shown that adreno-cortical insufficiency due to surgical trauma can appear when anaesthesia is ended.

Until all these problems are adequately elucidated it seems wise to agree with Burstein who recommends that "whenever there develops a condition of shock which is not due to manipulative circulatory reflexes and which does not respond to adequate blood replacement, the patient should be given the benefit of the doubt and should be treated with intravenous hydrocortisone."

Summary

This presentation has attempted to summarize the role of the adrenal cortex in health and disease. The medical conditions for which cortisone therapy has been employed have been listed, in order to alert the anaesthetist to the possibility of previous treatment with steroids in patients who are suffering or have suffered at any time from these diseases. The various tests for adrenal function are described, as are the treatment of adrenal cortical dysfunction, the complications of treatment, and contra-indications to steroid therapy.

The adrenals may be removed by the surgeon: (1) to influence secondary carcinoma; (2) to remove non-endocrine tumours of the adrenals; (3) to influence abnormal conditions of adrenal function manifested by hypersecretion of adrenal cortical hormones; (4) incidentally, in the course of operations on adjacent organs. In all these cases substitution therapy is necessary. It should be started preoperatively and may have to be carried on indefinitely.

Finally, the condition of "latent adrenal insufficiency" is described. This is a syndrome characterized by a shock-like state following major stress. It responds poorly to the usual measures adopted for shock, but is often dramatically influenced by the administration of large doses of adrenal cortical hormone. Prophylactic use of steroid therapy in suspect cases is advocated.

Résumé

Dans cet article, nous avons essayé de résumer le rôle du cortex surrénalien dans l'état de santé et au cours de la maladie. Nous avons énuméré les états pathologiques où l'on a employé la cortisone de façon à attirer l'attention de l'anesthésiste sur la possibilité d'un traitement antérieur aux stéroïdes chez des malades qui souffrent ou ont déjà souffert de ces maladies. Nous avons décrit les différentes épreuves de la fonction surrénalienne ainsi que le traitement des troubles corticaux surrénaliens, les complications du traitement et les contre-indications de cette thérapie.

On peut enlever chirurgicalement les surrénales: (1) pour agir sur un carcinome secondaire; (2) pour enlever des tumeurs non endocriniennes de la surrénale; (3) pour modifier des états anormaux de la fonction surrénalienne manifestés par une hypersécrétion d'hormones corticales; (4) incidemment, au cours d'opérations sur les organes voisins. Dans toutes ces éventualités, il faut instituer une thérapie de substitution. Il serait préférable de la commencer avant l'opération et il peut arriver qu'on doive la continuer indéfiniment.

Enfin, nous avons décrit l'état d'insuffisance surrénalienne chronique. Il s'agit d'un syndrome caractérisé par une sorte d'état de choc à la suite d'un stress important. On obtient peu de réponse aux traitements usuels du choc, mais il répond souvent, de façon étonnante, à l'administration de fortes doses d'hormones corticales surrénaliennes. Dans les cas douteux, il est même conseillé d'instituer une thérapie prophylactique aux stéroïdes.

ANAESTHESIA IN ADRENO-CORTICAL HYPERFUNCTION[1]

ALAN B. NOBLE, M.D.[2]

PATIENTS WITH adreno-cortical hyperfunction are not frequently presented to anaesthetists. The proper anaesthetic management for adrenalectomy in these cases requires a basic understanding of the physiopathology of the syndromes caused by hyperfunction of the adrenal cortex.

The adrenal cortex secretes three types of steroid hormones, the gluco-corticoids, and the mineralo-corticoids and hormones with androgenic and oestrogenic properties.

The majority of gluco-corticoids are in the form of hydrocortisone and cortisone, hydrocortisone being the main gluco-corticoid secreted. These hormones have been called "S" hormones because of their effect on carbohydrate metabolism, resulting in a decreased tolerance to carbohydrate and an increased tolerance to insulin.

Hydrocortisone and cortisone have also been labelled the anti-anabolic hormones since, by diverting amino-acids from gluconeo-genesis, they inhibit formation of body protein and eventually there is a marked deficiency of body protein.

The mineralo-corticoids regulate salt and water metabolism. Aldosterone which is the most important in man causes retention of sodium and elimination of potassium.

The androgens and oestrogens of the adrenal cortex contribute to the development of secondary sex characteristics. Excess of these steroids may lead to suppression of the gonad and distortion of secondary sexual development.

There is no clear-cut separation of the biological activities of these hormones. For example, androgens are salt retainers, but not nearly to the same degree as aldosterone. Cortisone is a poor mineralo-corticoid compared with aldosterone or even desoxy-cortico-sterone acetate. Due to the overlapping of biological activity, it is therefore not surprising that patients with adreno-cortical hyperfunction are often difficult to categorize clinically.

There are, however, three main syndromes of adreno-cortical hyperfunction which can be attributed to the three groups of hormones produced by the adrenal. These are Cushing's syndrome, virilizing adrenal hyperplasia and primary aldosteronism.

Overproduction of gluco-corticoids results in Cushing's syndrome and can be produced in man by the administration of cortisone in large doses.

In Cushing's syndrome, the influence of gluco-corticoids on carbohydrate metabolism is manifested clinically by hyperglycaemia and glycosuria, and these patients may be on fairly large doses of insulin. The anti-anabolic effect of the gluco-corticoids is manifested clinically by thin skin, easy bruisability due to increased friability of the blood vessels, and delayed wound healing. Deficient

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repair of bone matrix may lead to severe osteoporosis, and vertebral collapse is not uncommon. One of the most striking features of body protein depletion is muscle weakness and wasting. This may be dramatically demonstrated at operation. The loin incision will expose and proceed through much loose adipose tissue and expose a meagre erector spinae mass and later a diaphragm as thin as tissue paper. In addition, patients with Cushing's syndrome may have hypertension and oedema. The female patient may exhibit hirsutism, acne and amenorrhoea to such an extent that differentiation from adrenal virilism is difficult. In many cases such identification is of academic interest only. In Cushing's syndrome there is elevation of the 17-hydroxy-corticoids in the urine and the 17-keto-steroids may also be increased although usually not to the same degree. There may be derangement of the serum electrolyte pattern, with hypokalaemic, hypochloremic, hypernatremic alkalosis, although this is not common.

The commonest syndrome associated with overproduction of the gonadal-like hormones of the adrenal in the adult is virilizing adrenal hyperplasia in the female. This is characterized by hirsutism, amenorrhoea and not infrequently obesity. There may or may not be hypertension. There is elevation of the 17-keto-steroids in the urine, usually with slight or no elevation of the 17-hydroxy-corticoids.

Overproduction of mineralo-corticoids results in primary aldosteronism recently described by Conn (15).

The outstanding clinical finding is that of weakness with episodes of paralysis and tetany attributable to the severe depletion of body potassium that occurs. There is usually hypertension, which is apparently secondary to salt retention, although strangely there is no oedema.

During the past eighteen months we have had eight patients suffering from adreno-cortical hyperfunction presented for adrenalectomy. There were five patients with Cushing's syndrome and three with virilizing adrenal hyperplasia. This small number of cases is inadequate for compilation of a statistical analysis. Because cases of this type are being encountered sporadically by anaesthetists across the country, we feel justified in attempting a discussion of the anaesthetic problems involved. In addition, anaesthesia for adrenalectomy is always an exercise in the anticipation and treatment of emergency situations.

Two cases are presented as examples.

Case 1

The first case was that of an acute fulminating Cushing's syndrome in a 57-year-old man. A probable chromophobe adenoma of the pituitary had been diagnosed five years ago and he had not improved on deep X-ray therapy.

He was sent to Montreal early in January after a period of several weeks in hospital in New Brunswick. The last admissions were because of visual disturbances, swelling of the feet, polydipsia, polyuria and easy fatiguability. His hypertension had increased to 220/140 and he had consistently elevated blood sugars. He was obese, plethoric, with a moon-shaped face and excess fat on the face, shoulders and trunk, sparing the extremities. The skin was thin and inelastic and he had numerous ecchymoses and some purpuric spots on the abdomen. There was marked pitting oedema of the legs and the hands were slightly oedematous. The fundi showed a Grade III hypertensive retinopathy with increased light reflexes, A-V nicking, haemorrhages and cotton-wool exudates.

He was orthopnoeic with a persistent productive cough. Rhonchi were heard over the entire chest and there was definite evidence of congestion at the lung bases. The heart was slightly enlarged to percussion. He had episodes of auricular fibrillation.

The laboratory reports on this patient were voluminous and are summarized here: (1) urine showed persistent albuminuria; (2) variable Glycosuria occurred during diet and insulin therapy for his diabetes; (3) blood proteins were decreased—total protein 5.3 gm. per cent, albumin 3.4 gm. per cent, globulin 1.8 gm. per cent; (4) blood cholesterol was elevated to 492 mg. per cent; (5) endocrine assays showed elevated 17-hydoxy-corticoids

Electrocardiogram taken January 21, 1957, revealed left ventricular hypertrophy or alternatively, incomplete left bundle-branch block.

Early in the morning of January 26, the patient had an episode characterized by nausea, vomiting and hypotension, clinically simulating myocardial infarction. Serum electrolytes showed a hypochloremic alkalosis with a serum K of 2.9 mEq. He responded to KCL and electrolyte therapy.

We were asked to see the patient in consultation, and on January 29, Dr. Bromage wrote that he was reluctant to administer an anaesthetic because of the "difficulty in maintaining an adequate respiratory exchange during a long operative procedure in the prone position and during the immediate post-operative period. This would be aggravated by anticipated bronchospasm and secretions during surgery. If operation was imperative, the choice of anaesthesia would be combined continuous extradural block and light endotracheal anaesthesia, with a tracheotomy to be performed before leaving the Operating Room, in order to facilitate frequent tracheo-bronchial toilet. Continuance of the extradural block would provide analgesia for chest pain and result in more effective coughing."

We were advised that because of the fulminating state of his disease, bilateral adrenalectomy offered the only hope for the patient's survival, and the family were well aware of this and of the grave risk involved. On January 31 the patient underwent bilateral adrenalectomy, after preparation with cortisone. Hydrocortisone at the rate of 5 mg. per hour was given in an intravenous infusion during surgery. A reproduction of the anaesthetic chart is shown in Figure 1. The operation was uneventful.

At the point where the arrow marked "EEG" appears, the patient's electro-encephalogram showed diversion from a fast pattern associated with light anaesthesia to delta waves indicative of cerebral anoxia. This occurred in the absence of any clinical manifestations of hypoxia. The patient's colour, blood pressure, respirations and pulse rate showed no changes.

There was no evidence of respiratory obstruction and no audible evidence of secretions in the tube. For this reason aspiration through the endotracheal tube was delayed. The delta waves persisted. After three or four minutes the tube was aspirated and a considerable amount of tenacious mucus removed. Within a few minutes the normal rhythm of light anaesthesia was re-established. It was a striking example of the value of electro-encephalography.

At the completion of surgery a tracheotomy was performed.

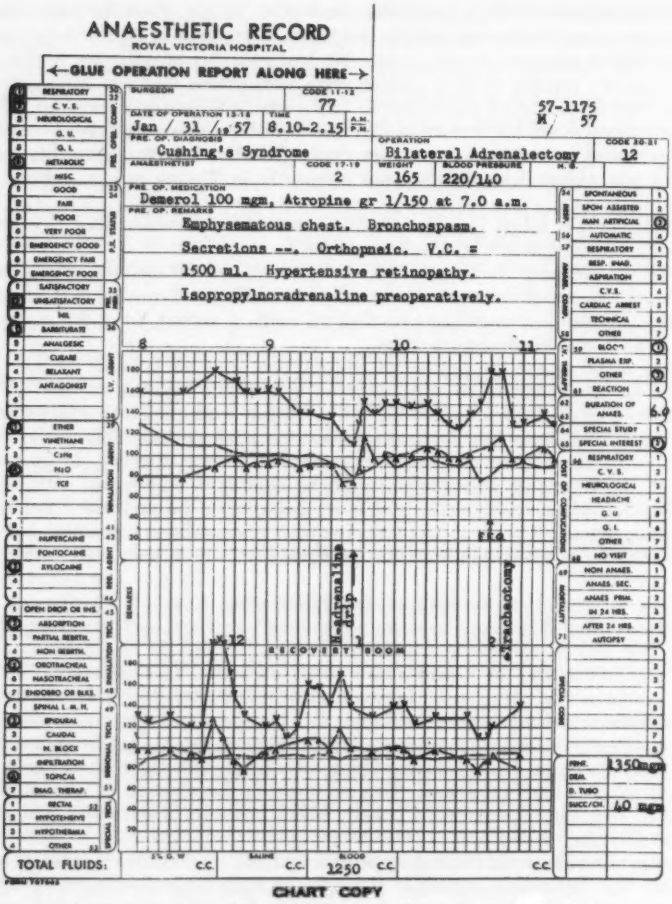
On moving the patient from the table, excoriation of the skin of the thighs was noted. We had not considered his tender skin and had allowed direct contact between the skin and the special supporting mattress. This is a lesson we have not forgotten.

The patient was kept under immediate supervision in the recovery room for 48 hours. Members of the resident staff attended him continuing on 4-hour shifts during this period in order to control secretions and supervise the administration of hydrocortisone, insulin, fluids and electrolytes.

Postoperatively the patient exhibited an exaggeration of his pre-existing psychosis. According to Starr, psychosis occurs in 65 per cent of patients with Cushing's syndrome.

The tracheotomy tube was removed on the seventh day. He was discharged three weeks after operation.

His insulin requirements dropped considerably after operation.


ANAESTHETIC RECORD
ROYAL VICTORIA HOSPITAL
←GLUE OPERATION REPORT ALONG HERE→
57-1175
M 57
Jan / 31 /19 57
8.10-2.15
Cushing's Syndrome
Bilateral Adrenalectomy
2
165
220/140
Demerol 100 mgm. Atropine gr 1/150 at 7.0 a.m.
Emphysematous chest. Bronchospasm.
Secretions --. Orthopneic. V.C. =
1500 ml. Hypertensive retinopathy.
Isopropylnoradrenaline preoperatively.
Adrenalin drip
Nembutal
Thiopentone
Succinylcholine
Pancuron
Flaxedil

There was a recent weight gain of 15–20 pounds. He developed nocturia and daytime frequency associated with abnormal thirst. Blood pressure was 240/160 with a pulse rate of 100. Fundi showed vascular tortuosity, A.V. nicking, and one small haemorrhage and some cotton-wool exudate were found in the right eye. Endocrine assay revealed elevated 17-keto-steroids and corticoids.

Anti-hypertensive drugs had very little effect and he was scheduled for bilateral adrenalectomy February 19, 1957. He was prepared with cortisone and moderate premedication. No conduction anaesthesia was used. He received intravenous Pentothal, Demerol, intracheal nitrous-oxide, oxygen and a relaxant. A polyethylene catheter was inserted in the right femoral vein. His anaesthetic chart shows that all went well until adrenal manipulation commenced.

The chart shows the hypertensive responses to this part of the procedure and the

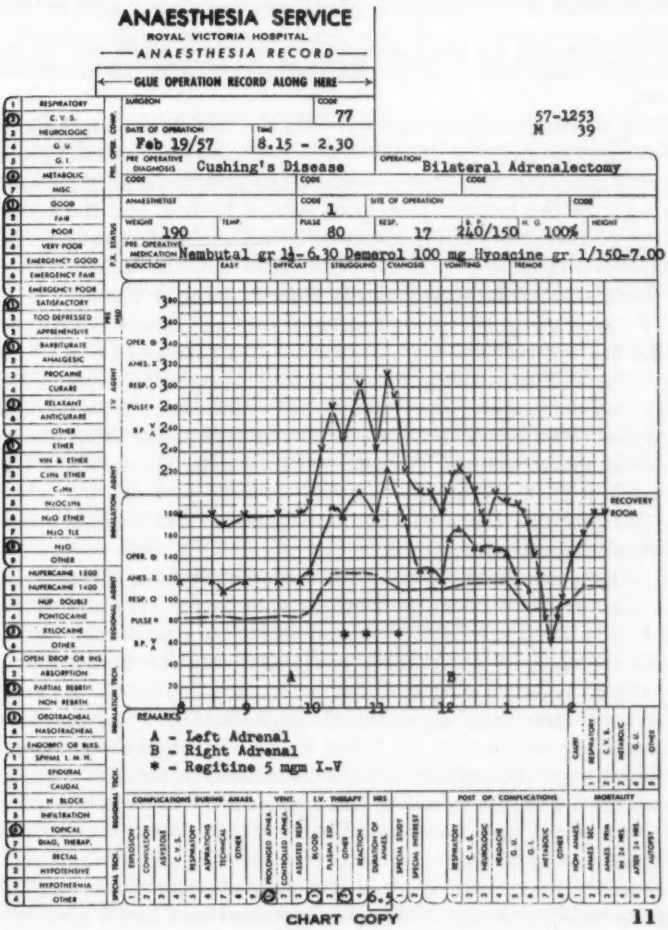


FIGURE 2. Anaesthetic record showing the hypertensive responses due to adrenal manipulation in Case 2.

incomplete reversal produced by 5 mg. doses of Regitine. Needless to say these episodes resulted in quite a distraction. As a result, inadequate attention was given to blood replacement during this period. The later hypotensive episode resulted when the inferior vena cava was accidently injured and active haemorrhage occurred.

During the immediate postoperative period he had a prolonged apnoea following a total dose of 950 mg. of succinylcholine over a 6-hour period. Adequate tidal exchange occurred following the intravenous administration of atropine, 0.4 mg. followed 5 minutes later by 1.5 mg. of prostigmine.

In the recovery room he appeared to be in good condition. He was rousing and maintaining his airway with no apparent difficulty. We left him. Within 5 minutes he suddenly became cyanosed and apnoeic. Fortunately, a staff member was nearby and he was re-intubated at once. He was extubated 10 minutes later and was conscious almost immediately. We have been unable to explain this episode satisfactorily. Eight days later he was re-anaesthetized uneventfully for removal of a pack in the right loin incision.

During convalescence his blood pressure was extremely labile and his response to antihypertensive drugs such as ansolysen rather unsatisfactory. He complained greatly of weakness.

According to our present knowledge, bilateral adrenalectomy offers the most effective method of arresting the metabolic dysfunctions in Cushing's syndrome. Surgeons are generally in favour of a one-stage procedure. In their opinion, this removes some of the hazards from poor wound healing and the low resistance to infection occurring in these patients. Bilateral exploration may reveal adrenal hyperplasia or functioning tumours. The latter may be benign or malignant. Adrenal carcinoma metastasizes slowly and if surgical removal is early, the chances of a cure are good. In some cases of frank Cushing's syndrome, bilateral exploration has not revealed any perceptible abnormality in the adrenals.

The two cases described reflect the anaesthetic problems involved. Some cases are not so well defined and may present manifestations of hypersecretion of one portion of the cortex. For instance, the results of hyper-aldosteronism may present the important manifestations. Preoperative preparation is carefully handled by the Department of Medicine, and we rely on their presence and advice during surgery. Our problem is one of alert management. The technical procedure of anaesthesia need not be stereotyped.

These patients are always obese with poor muscle tone. There may be fluid retention. Care must be taken to avoid pressure on the eyes and skin. The thin skin and friable blood vessels may be responsible for considerable difficulty with intravenous infusions. A polyethylene catheter should be inserted after cutting down on a large vein in the leg.

Most patients have been on a diabetic regimen. Diabetic acidosis is rare. If they are receiving insulin, they are better to come to surgery with some elevation of their blood sugar. Hypoglycaemic reactions must be avoided.

Osteoporosis is common. Many of these patients have spontaneous fractures of the vertebrae. Great care must be taken to avoid trauma to the spine during posturing and during surgery.

The prone position requires controlled or assisted respirations in order to assure an adequate tidal exchange and avoid hypercarbia. Careful tracheal toilet is essential. Controlled respirations with a cuffed tube are also necessary in case the pleura becomes accidentally torn during removal of the twelfth rib.

Mushin (2) correctly advocates readiness for dealing with hypertensive crises during adrenalectomy for any reason. The second patient described here reacted dramatically during the period of adrenal manipulation. It is well to point out that phaeochromocytomas are not the only suprarenal lesions responsible for these episodes.

Phentolamine (Rogitine) is the best adrenergic blocking agent for the treatment of these reactions. The effects are reliable and the agent should be readily available.

Adrenal insufficiency is a hazard. It is difficult to understand why a patient showing many of the signs of Cushing's syndrome can be potentially adrenal deficient, but Thorn (4) has pointed out that this can be the case and such people do not respond normally to stress. Marquardt (16) has also pointed out that, in this disease, adrenal hyperplasia may be associated with atrophy of the contralateral gland. This may be the result of ACTH inhibition by the overactive gland.

Perkoff *et al.* (7) found that hypotension was more common after surgery for Cushing's syndrome than after adrenalectomy for other reasons. For this reason Latham (8) recommends large doses of cortisone for patients with Cushing's syndrome.

This form of preoperative preparation and support during surgery should be ordered by the members of the medical staff and their presence during the surgical procedure is of great value in designating the amount of hydrocortisone required.

These patients were prepared with doses of up to 600 mg. of cortisone intramuscularly over a period of 60 hours before operation, followed by a final dose of 100 mg., by mouth, one hour before operation.

During operation, a continuous infusion of hydrocortisone .2 per cent was administered and continued during the recovery period. A total of 200 mg. was administered during the first twenty-four hours. This was reduced to 100 mg. during the second twenty-four hours.

Hypotension is most common immediately after removal of the adrenals and, of course, may occur in the presence of adequate cortisone.

Anaesthetic Management

(*a*) Premedication. These patients may have a potential adrenal insufficiency. Some years ago Thorn (4) warned against the low tolerance to opiates exhibited by patients with adrenal insufficiency. It is better to use Demerol in preference to morphine premedication.

(*b*) Dundee (5) has stressed the necessity for care in the use of Pentothal in patients with a decreased metabolic rate. We have not noted an abnormal depressant effect due to Pentothal in these patients.

(*c*) Ether anaesthesia should be avoided because of the diabetic tendency of these patients.

Of interest is a fact mentioned to us by Dr. Leroy Vandam recently. He has noted an increase in blood gluco-corticoid levels in volunteers during ether anaesthesia.

(*d*) Cyclopropane is contra-indicated because of the possibility of liberation of large amounts of endogenous adrenaline and noradrenaline.

(*e*) Conduction techniques are probably of value in blocking the afferent stimuli responsible for the reflex liberation of adrenergic substances and corticoids. This has been confirmed by Vandam (14). On the other hand both spinal and epidural anaesthesia may result in vasomotor instability.

Four of our patients received continuous epidural anaesthesia combined with intratracheal N_2O and O_2. The remainder received Pentothal, Demerol, intratracheal nitrous oxide and oxygen relaxants. One patient had a prolonged apnoea following succinylcholine.

Induction of all these patients has been time consuming. After induction with anaesthesia a cut-down is performed on a large vein in the leg before posturing the patient.

Patients are postured on a special mattress to avoid interference with respiratory function. Cortisone is administered by infusion into a wrist vein.

Recovery Room Care

Continuous postoperative care is required for these patients during this period. There are important considerations not encountered in the ordinary postoperative case. A continuous blood pressure chart must be kept and fluid balance carefully recorded.

Postoperative stability is a manifestation of adequate cortisone therapy. Under these circumstances adrenal crisis is rare (10), but should be suspected if vomiting, hypotension, hyperthermia and extreme weakness occur. Serum chemistry may not be confirmatory (7).

If this diagnosis is confirmed by medical consultation, hydrocortisone succinate, 100 mg., is administered over a four- to five-minute period. In cases of adrenal crises, prompt improvement will occur.

Postoperative haemorrhage must be watched for. Patients with adreno-cortical hyperfunction are obese, exposure is difficult and the area is vascular. The occurrence of hypotension with tachycardia and other manifestations of shock suggests possible haemorrhage. This condition was found in the second patient who was returned with a gauze pack in one incision.

Vasomotor instability may be revealed by hypotension. With adequate cortisone this is rare (10). It was not of serious consequence in any of our patients. Support with norepinephrine over a period of several hours is usually adequate.

There is a tendency towards over-zealous treatment with norepinephrine in order to maintain arbitrary blood-pressure levels. It is better to assess the patient's condition—general appearance, blood pressure, capillary refilling time and urinary output. Determining the latter may be difficult during the postoperative period of oliguria. The use of noradrenaline may present problems. After noradrenaline infusion of several hours duration, discontinuance may result in a sharp drop in blood pressure. This has been explained by Burn (11) and others as due to the ganglion-blocking effect of noradrenaline, which they have demonstrated experimentally. Cessation of the infusion decreases the vasoconstrictive effect of the noradrenaline while the ganglion-blocking effect persists.

resulting in hypotension. Burn advocates the use of vasopressin when the weaning from noradrenaline is difficult.

We have found a single intramuscular dose of 20 mg. of methoxamine of value in these cases. Methoxamine seems to maintain the vasoconstriction while the ganglion blockade resulting from norepinephrine is wearing off. Mushin (12) commented recently on this problem.

The total fluid intake during the day of surgery must be watched carefully. Over-hydration may result in hyponatremia or pulmonary oedema.

Pulmonary complications must be anticipated after prolonged surgery in the prone position with the added problems of obesity and poor muscle tone. One patient developed a right upper lobe broncho-pneumonia probably superimposed on an immediate atelectasis. The condition was suspected before he left the recovery room and responded to conservative treatment.

Résumé

L'on n'a pas souvent l'occasion d'anesthésier des patients souffrant d'hypercortico-surrénalisme. La bonne conduite de ces cas de surrénalectomie requiert une parfaite connaissance de la physiopathologie des syndromes d'hypercortico-surrénalisme.

La cortico-surrénale produit trois genres de stéroïdes: les gluco-corticoïdes, les minéralo-corticoïdes et des hormones androgènes et estrogènes. Les principaux gluco-corticoïdes sont la cortisone et l'hydrocortisone, appelées hormones "S" à cause de leur action sur le MB des hydrates de carbone. On les appelle aussi hormones anaboliques, car elles bloquent la gluconéogénèse à partir des acides-aminés et inhibent la formation de protéines dans l'organisme, ce qui a pour résultat une baisse marquée des protéines. Les minéralo-corticoïdes régularisent le MB de l'eau et du sel. L'aldostérone est la substance la plus importante de ce groupe: elle règle la rétention de Na et l'excrétion du K. Quant aux hormones androgènes et estrogènes, elles contribuent au développement des caractères sexuels secondaires.

Il faut dire que ces actions biologiques ne sont pas aussi nettement dissociées, les androgènes agissent aussi sur la rétention du sel. D'où la difficulté de différencier les syndromes d'hypercortico-surrénalisme.

On reconnait trois grands syndromes, correspondant à chacun des trois groupes de produits de la cortico-surrénale: le syndrome de Cushing, le syndrome adréno-génital et l'aldostéronisme primaire.

Le syndrome de Cushing vient d'une surproduction de gluco-corticoïdes. (L'injection de doses excessives de cortisone amène les mêmes résultats.) On y trouve de l'hyperglycémie, de la glucosurie, une fonte musculaire frappante, parfois de l'hypertention et de l'œdème ou, chez la femme, de l'hirsutisme, de l'acnée et de l'aménorrhée. On y trouve encore une élévation des 17-hydroxy-corticoïdes dans l'urine, parfois une augmentation des 17-kétostéroïdes, enfin une diminution du K, du Cl et du Na sanguins.

Le syndrome adréno-génital, ou virilisme surrénalien, provient d'une surproduction surrénalienne de substances gonadotropes. Il se rencontre le plus souvent chez la femme où il se caractérise par de l'hirsutisme, de l'aménorrhée, souvent

de l'obésité, de l'hypertension, une augmentation des 17-kétostéroïdes urinaires et des 17-HOGS.

L'aldostéronisme primaire, récemment décrit par Conn, provient d'un excès de minéralo-corticoïdes; il se manifeste ainsi: faiblesse, épisodes de paralysie et de tétanie due à une déficience marquée de K; hypertension apparemment secondaire à une rétention de Na, mais sans œdème.

Depuis dix-huit mois, nous eûmes à anesthésier pour surrénalectomie huit cas d'hypercortico-surrénalisme, dont cinq syndromes de Cushing et trois syndromes adréno-génitaux. La rareté de ces cas et surtout leur intérêt majeur pour les anesthésistes justifient la présentation de cet article.

Voici deux de ces cas.

Premier cas

Syndrome de Cushing suraigu: homme de 57 ans présentant polydypsie, polyurie, hypertension artérielle, faciès lunaire, obésité localisée à la face, aux épaules et au tronc, mais non aux extrémités, congestion des bases pulmonaires, peau mince, dépourvue d'élasticité, œdème à godet des jambes, orthopnée, toux productive persistante, psychose aiguë, hyperglycémie, pléthore sanguine, hypoprotéinémie, hypercholestérolémie, augmentation des 17-hydroxy-corticostéroïdes.

A cause de l'état cardio-pulmonaire du patient et à cause de l'opération (surrénalectomie bilatérale), il eut comme anesthésie une épidurale continue associée à une anesthésie endotrachéale légère. A la fin de l'opération, une trachéotomie fut faite pour faciliter l'aspiration bronchique.

Les résidents se relayèrent pour surveiller étroitement le traitement et les suites post-opératoires, qui ne furent marquées d'aucun incident.

Deuxième cas

Patient de 39 ans admis une première fois en 1950 pour syndrome de Cushing; réadmis en 1957; obésité tronculaire, hypertension grave, augmentation des 17-kétostéroïdes, courbe positive d'hyperglycémie provoquée.

Il subit une surrénalectomie bilatérale sous anesthésie générale: Pentothal, protoxyde d'azote, curare. Une crise d'hypertension provoquée par les manipulations chirurgicales fut en partie contrôlée par des doses de 5 mg. de Régitine. A la fin de l'opération, il eut une apnée prolongée: il avait reçu 950 mg. de succinylcholine pendant une période de 6 heures. Cette apnée fut corrigée par de l'atropine 0.4 mg. i-v, suivie de prostigmine 1.5 mg. après 5 minutes.

Pour résumer, les problèmes qui se posent à l'anesthésiste sont les suivants: obésité, asthénie, hypertension, congestion pulmonaire, surcharge liquidienne, fragilité des tissus, des vaisseaux et des os, crises hypertensives per-opératoires, hypotension post-opératoire, position ventrale, durée prolongée de l'intervention, nécessité d'une surveillance post-opératoire étroite et prolongée.

Dans les crises hypertensives, c'est le phentolamine (Régitine) qui agit le mieux comme sympatholytique.

L'insuffisance surrénalienne post-opératoire est toujours à craindre, car ces patients répondent mal au stress, surtout chez les syndromes de Cushing.

Ces patients reçurent de fortes doses de cortisone avant l'opération et une solution d'hydrocortisone 0.2% pendant et après l'intervention.

Conduite anesthésique

(1) Prémédication: Démérol de préférence à la morphine.

(2) Induction: Pentothal, à dose prudente.

(3) Maintien: éviter l'éther à cause de l'hyperglycémie; éviter le cyclopropane qui pourrait libérer de fortes doses d'adrénaline et de nor-adrénaline.

Les techniques d'anesthésie par conduction ont probablement de la valeur par leur action sympatholytique, mais la rachi et l'épidurale peuvent amener une instabilité vasomotrice.

Quatre de nos patients eurent une épidurale continue associée au N_2O. Les autres reçurent du Pentothal, du Démérol, du N_2O et du curare.

(4) Soins à la salle de réveil: surveillance continue et enregistrement précis de la T.A., des liquides.

La stabilité de la T.A. sera le signe d'un traitement adéquat à la cortisone. Il faut soupçonner une déficience de ce côté, en cas de vômissement, d'hypotension, d'hyperthermie et d'extrême faiblesse. Alors, le succinate d'hydrocortisone 100 mg. en 4 à 5 minutes agit bien.

Il faut aussi avoir l'œil ouvert sur la possibilité d'hémorragie dans la plaie, à cause de sa riche vascularisation.

L'hypotension peut venir aussi de l'instabilité vasomotrice. La nor-adrénaline en goutte à goutte pendant plusieurs heures après l'opération soutiendra la T.A. Il faut cependant en restreindre la quantité car la nor-adrénaline semble posséder aussi une action ganglioplégique qui peut se manifester par de l'hypotension aiguë quand on la cesse. La méthoxamine (20 mg. i-m) agit bien contre cette complication.

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POSTOPERATIVE TREATMENT WITH ARTIFICIAL RESPIRATION OF TWO THORACIC SURGICAL PATIENTS[1]

J. G. ROBSON, F.F.A.R.C.S. (ENG.)[2]

THE USE OF artificial respiration in the postoperative period for tuberculous patients was reported on by Björk and Engström (1). When acute infection occurred in the only functioning lung of two of their patients, they maintained artificial respiration for six and nine days, and both patients recovered.

The following report may be of interest to anaesthetists because of the growing use of such methods and it illustrates the application of prolonged artificial and assisted respiration without the necessity for complicated biochemical control.

The first patient was a woman of 46 with a long history of pulmonary tuberculosis. In 1939 she had a seven-rib thoracoplasty for closure of a right apical cavity. Closure was not complete and her sputum intermittently contained tubercle bacilli thereafter. Fourteen years later (1953) a lesion developed on the left side which was controlled by chemotherapy. When this had healed, in 1956, it was decided to remove the right lung to prevent re-infection.

Pneumonectomy proved to be very difficult. The bony chest wall was composed of plaques of regenerated bone, much of which had to be removed in order to mobilize the lung. Closure of the chest was necessarily inefficient.

The postoperative course was stormy. With the very deficient chest wall, mediastinal movement was gross and coughing was mechanically almost impossible. She had attacks of great respiratory distress caused by the accumulation of secretions, but by the fourth day she was fairly well. During this period she was febrile. On the tenth day her condition rapidly deteriorated. The respiratory rate increased to between 40 and 50 per minute, she again had fever and she was at times disorientated. By the eleventh day she was comatose, flushed, cyanosed and sweating and obviously had marked carbon dioxide retention with anoxia. The arterial oxygen saturation was 65 per cent, carbon dioxide content 97 vol. per cent (arterial blood) and the blood Ph was 7.3 Chest X-ray showed that there was patchy consolidation in the mid-zone of the remaining lung and that the heart had moved over to the left. The pulmonary infection following mechanical inefficiency of respiration had precipitated respiratory failure.

During transit to the operating theatre respiration ceased and orotracheal intubation was performed while she was making only an occasional anoxic gasp. She recovered consciousness after some thirty minutes of hyperventilation with oxygen. Four hours later, when her general condition had improved sufficiently, tracheostomy was performed under light cyclopropane anaesthesia. A cuffed cut-down Magill rubber tube no. 9 was inserted into the stoma and intermittent positive/negative pressure respiration was continued with a respirator.

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The respirator used was one described by Horton, Inkster and Pask (2). This machine is a pressure cycling device which provides positive and negative phases and has a patient-controlled demand valve which allows the delivery of gas to the pre-set pressure of the exertion of about 1 cm. water negative pressure by the patient. The machine was at first supplied through an entraining device from oxygen cylinders, the gas mixture containing about 50 per cent oxygen. With this mixture a pressure differential of 35 cm. water, 25 positive, 10 negative, at a cycling rate of 40 per minute was required, in order to keep the patient a reasonable colour. Gas exchange was so poor that the functioning lung had to be worked to this extreme degree. Such pressures would not have been required had pure oxygen been used, but the attainment of a reasonably high minute volume for the clearance of carbon dioxide was of major importance.

Within a few hours the chest wall on the right had become convex and showed little movement and the heart had moved over to the right. By the second day the arterial blood oxygen saturation was 96 per cent, carbon dioxide tension 40 mm. mercury, carbon dioxide content 73 vol. per hundred and Ph 7.5. Her respiratory rate had by this time been reduced to 20–22 per minute and the negative phase was therefore discontinued. Respiratory control was from then on fairly simple. The positive pressure, and so the tidal volume, were reduced progressively until spontaneous respiration returned and the cycling rate was adjusted until it equalled the patient-triggered rate. The pressure was then slowly increased until apnoea once more just supervened. This process was carried out twice a day and it avoided the necessity for repeated blood gas estimations. This patient was very sensitive to the oxygen content of the supplied mixture and would not tolerate artificial respiration with air alone until the eighth day. On the same day a fall in temperature and pulse rate indicated resolution of the pulmonary infection. X-ray at this time showed the left lung to be clear of infection and the heart in the normal position. The efficient removal of secretions and the prevention of pulmonary collapse were of vital importance and a conscientious regimen of posturing with chest percussion and tracheo-bronchial aspiration was followed. Secretions were kept fluid and easy to aspirate by efficient humidification of the gases. The patient's feeling of well-being, the pulse rate and blood pressure, reflected the efficiency with which this routine was carried out. The cuff of the tracheal tube was deflated for one minute every two hours and no symptoms of tracheal pressure developed. The tube did not require to be changed during the treatment.

By the twenty-eighth day, the chest wall had become rigid enough for the artificial respiration to be discontinued. "Weaning" presented no difficulties. The tracheostome healed normally and the patient left the hospital well.

The second patient was a man of 56 with a history of pulmonary tuberculosis for two years. On admission he had a complete tuberculous excavation of his right upper lobe. In December, 1955, the right upper lobe and the apical segment of the lower lobe were resected, this being technically very difficult. During a difficult convalescence he developed an empyema with a broncho-pleural fistula and this was drained.

In February, 1956, an upper four-rib thoracoplasty was performed as the

closure of the fistula seemed to offer the only chance for his survival. Postoperatively he required repeated bronchoscopy as he was unable to cough effectively. The subscapular space, being in communication with the empyema space, became infected. His general condition progressively deteriorated and on the third postoperative day he presented a picture of gross carbon dioxide retention and anoxia. He was intubated without further anaesthesia, much pus was aspirated from his bronchial tree and he was artificially ventilated with the respirator. Within six hours he had improved so markedly that it seemed to be worthwhile to persist with artificial respiration and a tracheostomy was performed. Acclimatisation to the machine was very easy as this patient much appreciated the value of the sparing of his own efforts.

In the course of the next three weeks he nearly drowned many times as pus from the subscapular and empyema spaces flooded into his bronchi. The respirator was adjusted as described earlier and from time to time it was discontinued for short periods. During these spells of spontaneous respiration his condition became worse despite continued removal of secretions. General nursing was very difficult as he was so emaciated. His wound broke down despite minute care. With good metabolic supervision and repeated blood transfusion, his condition improved sufficiently for artificial respiration to be discontinued on the twenty-first postoperative day. A plugged tracheostomy tube was kept in place for the next two weeks to allow aspiration of his secretions. He died at this time from a coronary thrombosis, a large myocardial infarct of recent origin being demonstrated at autopsy.

Discussion

Björk and Engström note that in patients with a very low respiratory reserve, when acute infection develops in the functioning lung, marked increases in the rate of respiration above normal are required and the pressure differential sometimes needs to be high. This was the case with the first patient.

A tracheostomy alone will reduce the dead space by about 100 cc. and this of itself may be sufficient to allow effective carbon dioxide clearance in some patients. In the first patient it was quite obvious that the best chance of her survival lay in the encouragement of fixation of the chest wall and intermittent positive pressure respiration was the method of choice. The second patient was physically too weak either to cough up his secretions, or to breathe efficiently even through a tracheostomy, for the first three weeks after the institution of artificial respiration, so that decision was not difficult.

When any doubt exists about the employment of artificial respiration, the therapeutic test of oral intubation and manual artificial ventilation is the obvious way to reach a decision.

Summary

This paper describes the prolonged treatment by intermittent positive pressure respiration through a tracheostomy of two patients who developed respiratory failure following operation.

One patient had a seven-rib thoracoplasty on the right side and, because of subsequent infection of her left lung from the incompletely closed cavity under the thoracoplasty, had a right pneumonectomy. Following this the right chest wall was completely lax so that respiration and coughing were inefficient. Acute infection developed in the lung and respiratory failure followed. Treatment was by artificial respiration for twenty-eight days through a tracheostomy using an intermittent positive-negative pressure respirator which had a patient demand valve. The chest wall became firm and recovery followed.

The second patient developed a broncho-pleural fistula following right upper lobectomy for a tuberculous excavation of the right upper lobe. This was treated by thoracoplasty. Respiratory failure followed and he was treated by intermittent positive pressure respiration for twenty-one days. He died twenty-one days later from myocardial infarction.

Résumé

Dans cet article, nous faisons l'exposé du traitement prolongé de deux malades qui, à la suite d'une opération, ont fait un arrêt respiratoire et, après trachéotomie, ont été soumis à une respiration artificielle à pression positive intermittente.

Le premier de ces malades avait subi une thoracoplastie droite de sept côtes et, à cause d'une infection subséquente de son poumon gauche par la cavité droite incomplètement fermée par la thoracoplastie, a dû subir une pneumonectomie droite. Après ces opérations, la paroi thoracique droite était complètement flasque de sorte que la respiration et la toux étaient insuffisantes. Le poumon restant s'est infecté et la respiration a cessé. Le traitement a consisté en une respiration artificielle durant 28 jours et cela par la trachéotomie. On s'est servi d'un respirateur à pression positive et négative intermittente qui était muni d'une valve à demande. La paroi thoracique s'est solidifiée et la guérison a suivi.

Le deuxième malade a fait une fistule bronchopleurale à la suite d'une lobectomie supérieure droite pour une cavité tuberculeuse du lobe supérieur droit. Le traitement a consisté en thoracoplastie. L' arrêt respiratoire est survenu et il a été traité, durant 21 jours, par une respiration artificielle à pression positive intermittente. Il mourut d'un infarctus du myocarde 21 jours plus tard.

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THE PHRENIC REFLEX IN EPIDURAL ANALGESIA

P. R. BROMAGE, M.B., B.S., F.F.A.R.C.S.[1]

AN ALTERATION of certain respiratory reflex patterns appears to accompany high subarachnoid or extradural spinal blockade. Attention has been drawn to the release of bronchospasm which often occurs in bronchospastic patients after induction of a high epidural block (1), and it has been shown that the vital capacity may increase by over 30 per cent in these patients (2).

In addition to release of bronchospasm, a modification of the diaphragmatic reflex also occurs. I noticed that in thoraco-abdominal operations carried out under a combination of a light general anaesthesia and epidural block to T_2, the diaphragm would remain unreactive even though the surgical incision extended to the central part of the diaphragm. Failure to respond to direct diaphragmatic stimulation in the presence of an intact reflex arc (through C_3, C_4 and C_5), invited closer attention, and this paper is concerned with further clinical observations on the phenomenon of associated phrenic suppression.

METHOD

Fifty-two patients undergoing thoracotomy were anaesthetized by a combination of continuous epidural analgesia and light general anaesthesia in such a way that airway control could be assured throughout the operation, while at the same time anaesthesia was light enough to determine the upper level of segmental analgesia with fair accuracy. The upper level of analgesia was tested by pinprick or pinching the skin after induction of the epidural block and during and immediately after operation. The following segmental landmarks were adopted, compromising between the dermatome maps of Foerster (3) and Keegan (4):

T_4 Fourth intercostal space in axillary line
T_3 Third intercostal space in axillary line
T_2 Skin of thoracic wall of axilla
T_1 Skin of inner side of upper arm above elbow
C_8 Ulnar border of forearm and little finger
C_7 Not tested owing to possibility of overlap between C_6 and C_8
C_6 Thumb and radial border of forearm

During the course of operation, the surgeon was asked to stimulate the central portion of the diaphragm by pinching with a haemostat, and then to stimulate the phrenic nerve by light pinching while any associated movements of the diaphragm were observed.

Anaesthetic Procedure

Premedication was moderately heavy, usually with Pentobarbital 100 mg. two hours before operation, followed by Demerol, 50 to 100 mg., and atropine, 0.4 mg.,

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[2]Dosage for lidocaine (ml.) = [Height in inches + 10% + 3 times the number of spinal segments to be blocked above the vertebral level of injection] − [(Age in years ÷ 3) + 47] × 0.6 (1, p. 81).

one hour before operation. An epidural catheter was inserted in any convenient space between T_{10} and L_3, and analgesia induced with lidocaine (Xylocaine), 1.5 per cent without adrenaline. Dosage was based on a formula for the dosage of 1/600 nupercaine, reduced by a factor of $\times$ 0.6 to allow for the extra spreading tendencies of lidocaine (1).[2] Any fall of blood pressure was corrected by small doses of d-methyl amphetamine (Methedrine). Twelve to twenty minutes later the upper level of skin analgesia was tested by pin-prick. The level of the epidural block was maintained by giving half the volume of the initial dose every fifty to sixty minutes.

The laryngeal and tracheal reflexes were obtunded by a transtracheal injection of 2–3 ml. of 4 per cent lidocaine, and anaesthetic sleep induced with 2.5 per cent thiopental. Before and during induction of anaesthesia the patient was instructed to relax his face and neck muscles; this was of considerable help in providing relaxation of the jaw without the aid of a muscle relaxant for tracheal intubation. At this point bronchoscopy and endobronchial intubation were carried out if indicated by the nature of the pulmonary lesion. A cuffed endotracheal tube was gently inserted, and light anaesthesia maintained with five litres of nitrous oxide and two litres of oxygen per minute with CO_2 absorption. Further increments of thiopental were given, if necessary, to keep the patient from moving his head and arms during the operation. Controlled apnoea was induced by gentle hyperventilation, and under these circumstances the patient usually surrendered his spontaneous respiratory rhythm after five or ten "squeezes" of the respiratory bag. Minute volumes of 12–15 litres per minute were imposed. When a mechanical respirator was used the setting of the inspiratory pressure phase and the respiratory rate were determined by carrying out a few compliance readings before the start of operation. These were done by measuring the expiratory volume over an inspiratory pressure range of 10–20 cm. H_2O. Towards the end of operation epidural analgesia was maintained with a 0.8 per cent lidocaine solution instead of the 1.5 per cent solution to ensure that there would be minimal intercostal motor depression in the early postoperative period. The patients were awakened at the end of operation just before the skin sutures were completed, and the upper level of analgesia again checked.

A control series was attempted in eight other cases using the same general anaesthetic technique, but omitting the epidural block. The results were unsatisfactory. Respiration became uncontrollable, and a muscle relaxant had to be given to subdue the patients. In a few others a muscle relaxant was given at the outset, and the effect allowed to wear off when the chest was open. Diaphragmatic movements returned in these patients also, and operating conditions became intolerable, requiring further increments of muscle relaxant.

Results

Anaesthesia was remarkably smooth. Patients with existing bronchospasm showed improvement after the block.

Once apnoea was imposed by hyperventilation, the diaphragm remained relaxed and tranquil despite being rubbed, cut or stitched. Stimulation of the

central portion by pinching with a haemostat elicited only a localized sluggish fasciculation, but no co-ordinated contraction. On the other hand, stimulation of the phrenic nerve did elicit a fully co-ordinated contraction.

Owing to the exigencies of a busy operating theatre it was not possible to obtain accurate sensory levels in more than 31 of the 52 patients. The distribution of these levels is shown below.

Upper analgesic dermatome	*No. of cases*
C_6	3
C_7	–
C_8	5
T_1	8
T_2	10
T_3	4
T_4	1

It is probable that most of the remaining cases showed a similar sort of distribution, and certainly none were found to have analgesia extending as high as C_4.

Discussion

The observations on the behaviour of the diaphragm require interpretation and explanation, since it is not immediately apparent why the diaphragm should remain tranquil when the central portion is stimulated in the presence of an intact reflex arc mediated through the phrenic roots of C_3, C_4 and C_5. For although a block to T_2 will effectively interrupt sensations travelling in the dorsal roots of the lower six or seven intercostal nerves from the periphery of the diaphragm, the phrenic roots remain untouched.

If we concede that the sensory levels shown above were observed accurately, and that anaesthesia did not extend higher than C_8 in most cases, then two possibilities exist: (1) the innervation of the diaphragm is not so clear cut as is commonly believed; or (2) a functional reciprocation exists between the reflex patterns of the chest wall and those of the diaphragm of such delicate balance that suppression of the one is followed by suppression of the other.

The segmental motor supply of the diaphragm can vary within fairly wide limits. Kuré claimed that sympathetic efferents were partly responsible for diaphragmatic tone (5), but more recent work leaves little doubt that the motor supply is entirely confined to the spinal outflow from the phrenic nucleus (6). The commonest site of the phrenic motor nucleus is C_3, C_4 and C_5, but occasionally fibres may arise from any segment between C_1 and T_1, (8, 9, 10). Therefore, some degree of phrenic impairment might be expected in a small proportion of patients receiving a spinal block to C_6. However, in this series few of the blocks extended above C_8, and so it is unlikely that partial motor block of the phrenic nerve could have accounted for the observed diaphragmatic immobility during thoracotomy. Moreover, spontaneous diaphragmatic respiration was unimpaired except when apnoea was imposed by hyperventilation.

Since the motor side of the diaphragmatic reflex arc was not interrupted, it follows that diaphragmatic immobility must have been due to depression of either the afferent or the central components of the phrenic reflex arc. However,

there appeared to be little central depression of reflexes from other areas above the upper level of analgesia, since anaesthesia was so light that pinching the skin over the neck and shoulder would elicit a grimace or movements of the hand; so it may be assumed that the central components of the phrenic reflex were equally unaffected by the depth of anaesthesia. The unsatisfactory anaesthetic conditions in the control cases confirms that the combination of narcosis and hyperventilation did not produce sufficient central respiratory depression to abolish spontaneous diaphragmatic activity.

The afferent side of the phrenic reflex arc remains to be considered. About one-third of the fibres running in the phrenic nerve are sensory, the proportion of unmyelinated to myelinated sensory fibres being unusually high compared with other motor nerves (11). The reason for this unusual proportion is not clear, although a partial explanation may lie in the presence of a certain number of unmyelinated sympathetic afferents which travel with the phrenic nerve for varying distances (12). Cerebrospinal afferents reach the phrenic nucleus through the dorsal roots of C_3, C_4 and C_5 as well as C_6 (13), but these, like the motor outflow, would have been above the level of epidural block, although under the circumstances their influence proved ineffective.

Other afferents whose branches could play upon the phrenic nucleus in their passage to the brain stem would include sensory fibres from the thoracic wall and visceral afferents from the lungs, chest and abdomen. These latter appear to have some influence on diaphragmatic contraction, and Cromer and Ivy claim that their section reduces diaphragmatic tone (14). It is these sensory components which are eliminated by the type of block used in this investigation.

From the above evidence, one is led to the conclusion that phrenic reflex activity is normally dependent upon the summation of a number of different sensory stimuli, and that depletion of part of the total afferent neuronal "pool" leads to depression of the phrenic spinal reflex. Normally this neuronal "pool" will be fed by contributions from the upper sympathetic rami carrying impulses from the lungs and thoracic wall (15, 16, 17), together with cerebrospinal afferents from the thoracic cage. The effect of these is magnified because they act on the phrenic nucleus in two stages, directly, and by long projection pathways through the respiratory centre. Thus their elimination will have a correspondingly exaggerated effect in raising the threshold of the phrenic nucleus to such a level that the remaining incoming pathways cannot carry a sufficient volume of stimuli to produce a motor response.

For reasons of simplicity the phrenic reflex has been regarded in isolation from other related effects produced by high spinal block. Among these, modification of broncho-motor reflexes are of prime importance in the total picture of anaesthetic tranquillity and their study will form the subject of a separate communication.

Summary

Reflex response to stimulation of the central portion of the diaphragm is abolished by light general anaesthesia and epidural blockade to a level below C_5. The reasons for this are discussed.

Résumé

Cinquante-deux malades ont subi une thoracotomie sous anesthésie épidurale lombaire, combinée à une anesthésie générale superficielle, utilisant du pentothal, du protoxyde d'azote et de l'oxygène par voie endotrachéale. L'analgésie épidurale fut administrée à l'aide d'une solution de Xylocaine à 1.5% à travers une sonde en matière plastique (vinyl), insérée dans un espace interépineux approprié entre T_{10} et L_3. La limite supérieure de l'analgésie fut maintenue entre C_6 et T_4, afin d'épargner les racines mortices et sensitives du nerf phrénique et de conserver ainsi une mobilité diaphragmatique normale et spontanée. L'apnée fut obtenue par hyperventilation.

En de pareilles circonstances la region périphérique du diaphragme est insensibilisée, la région centrale par contre (innervée par les troisième, quatrième et cinquième nerfs cervicaux) garde sa sensibilité et réagit à l'excitation directe. Cependant une excitation directe de la région centrale du diaphragme durant l'opération ne réussit pas à déclencher une contraction coordonnée, quoique la stimulation du nerf phrénique lui-même y parvenait facilement. Une série-contrôle sous anésthesie générale superficielle, mais sans bloc épidural, répondit par une contraction extrèmement vigoureuse a l'excitation de la région centrale du diaphragme.

Afin d'expliquer les observations sus-jacentes, l'hypothèse suivante est émise:

Le réflexe phrénique est déclenché par la somme de différentes excitations périphériques, réalisant une sorte de "pool" nerveux. Toute diminution d'un affluent, alimentant ce "pool," entraîne une dépression de réflexe diaphragmatique, puisque le seuil de contraction ne peut plus être atteint. Le "pool" nerveux est normalement alimenté par des apports formés des ramifications sympathiques supérieures, transmettant les excitations des poumons et de la cage thoracique, ainsi que des fibres médullaires afférentes de la cage thoracique et de la plèvre pariétale. Quand les excitations périphériques, transmises par ces nerfs, sont abolies par une anesthésie épidurale haute, le seuil de contraction diaphragmatique ne pourra plus être atteint à l'aide des seules excitations transmises par les fibres afférentes du nerf phrénique.

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SEDATION OF CHILDREN FOR CARDIAC CATHETERIZATION WITH AN ATARACTIC MIXTURE[1]

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A VARIETY OF METHODS for producing satisfactory conditions for diagnostic cardiac catheterization and angiocardiography have been described (1, 2, 3, 4). We consider a satisfactory state is one in which there is (*a*) freedom from pain, (*b*) absence of restlessness throughout the entire procedure, (*c*) no respiratory depression, and (*d*) sedation light enough to allow a normal response to a selective ether test. The first condition may be satisfactorily achieved by infiltration of the cut-down site with procaine HCl. The latter three conditions have been achieved, with a high degree of dependability, by the intramuscular injection of a mixture of chlorpromazine, promethazine HCl and Demerol in a series of 670 infants and children.

Prior to February, 1954, a combination of Seconal and Demerol was used for sedation at the Hospital for Sick Children, Toronto. The deficiencies of this method were (*a*) an undependable degree of sedation, (*b*) restless during the study, and (*c*) a shocked appearance in many patients at the termination of catheterization, despite adequate blood replacement. In view of our satisfying experience with chlorpromazine and promethazine as preoperative sedatives (5), we considered that these agents might find a place in the sedation of patients for cardiac catheterization.

Chlorpromazine and promethazine given singly, together, and with various amounts of Demerol were administered to 80 patients. The ataractics alone improved the condition of patients at the termination of catheterization, but did not provide satisfactory conditions during the studies. The combination of Demerol with the ataractics (our "Catheter Mixtures") provided both optimum working conditions and a satisfactory post-catheter condition (Table I). The most dependable results were obtained with Catheter Mixture Number Three, CM_3, which contains the highest concentration of Demerol.

TABLE I

COMPOSITION OF "CATHETER MIXTURES"

	Proportions by volume						Mgm./cc. of mixture		
	Chlorpromazine		Promethazine		Demerol		Chlorpromazine	Promethazine	Demerol
CM_1[a]	1	:	1	:	1		8.3	8.3	16.7
CM_2	2	:	2	:	3		7.1	7.1	21.3
CM_3	1	:	1	:	2		6.25	6.25	25.0

[a]CM_1 = Laborit's Mixture One (M_1) (7).

CM_3 has been used on 670 patients, ranging in age from 4 days to 16 years; 43 per cent of the patients in the series were under one year of age.

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Age	*Number of cases*
Under 1 month	35
1–11 months	258
1–4 years	177
5–9 years	135
10 years and over	65
	670

Dosage

CM_3 was administered intramuscularly one hour before catheterization. The dose was based on the general condition of the patient and the degree of cyanosis. Acyanotic children in good general condition received 1 cc. of the mixture for each 20 pounds of body weight. In generally debilitated or cyanotic patients the dose was reduced by approximately 25 per cent. Large intramuscular injections are usually painful; and older patients usually require less sedation and are more co-operative. Accordingly, the dose was restricted to 1.5 cc. in patients weighing more than 30 pounds. When additional sedation was required, 25–50 per cent of the intramuscular dose was injected intravenously via the catheter. Only one patient required repeated supplementation during catheterization.

Pre-Catheter State and Complications

The pre-catheter conditions of each candidate was judged to be "good," "fair," or "poor" on the basis of (*a*) general nutrition and weight for age, (*b*) cardiac size, (*c*) presence of failure, (*d*) the degree of oxygen unsaturation at rest, and (*e*) the decrease in saturation accompanying exercise or crying. Using these criteria we judged that 214 patients were in good condition, 366 patients in fair condition, and 90 in poor condition.

Three subjects developed serious respiratory depression within one hour of the administration of the mixture. Two were cyanotic infants who received CM_3 on the basis of 1 cc./20 lb. The course of one of these patients is described under the section on mortality. The other patient responded promptly to treatment with Nalline.

Such reactions in cyanotic infants, we now appreciate, can be avoided by reducing the dose of CM_3 by 20–50 per cent depending on the degree of cyanosis.

A third non-cyanotic child weighing 43 lb. received 3.5 cc. of CM_3 in error and deve'oped marked respiratory depression. Catheterization was postponed until respiration became normal about three hours later.

Efficacy of Sedation

The majority of patients, 504, were well sedated and tolerated the entire procedure without becoming restless. Restlessness during the cut-down and insertion of catheter was encountered in 166 patients, 122 of whom became quiet and co-operative immediately following the insertion of the catheter. The remain-

ing 44 continued to cry and move about. Of these patients 26 were supplemented with small additions of CM_3 via the catheter and became well sedated; the remaining 18 (2.7 per cent) were not supplemented and constitute the failures in sedation encountered using CM_3. These cases occurred early in the series before injection through the catheter was considered to be a safe procedure.

One child, who had suffered a recent head injury, was extremely agitated before sedation and required three supplements during a study lasting two hours.

The duration of efficacy of CM_3 may be inferred from the following figures.

Duration	*Number of cases*
Under 1 hour	95
1–1½ hours	273
1½–2 hours	214
2–2½ hours	66
2½–3 hours	19
Over 3 hours	3
	670

The initial injection was quite adequate for times up to 3½ hours. The median duration of time for catheterization for the series was 81 minutes.

Condition during Catheterization

The majority of patients dozed from time to time during the procedure. They could always be easily awakened, and the older patients were able to chat with the attending nurses. Many patients exhibited a characteristic "smacking" movement of the lower lip. This phenomenon is an indication of excellent sedation, for all patients exhibiting this sign were completely free from all restlessness yet had no respiratory depression.

Depressed breathing did occur in one patient, a 20-lb. infant, following the intravenous injection of 0.5 cc. of CM_3. The depression was rapidly corrected by the injection of 0.12 cc. Nalline.

Although some patients exhibited a fall of 5–10 mm. Hg in mean pressure, the systemic blood pressure was not consistently lowered. Pulmonary artery pressures in a series of patients catheterized without sedation changed by only a few mm. Hg when CM_3 was injected intravenously (6).

The administration of CM_3 did not protect the heart against the occurrence of irregularities incident to manipulation of the catheter within its chambers. Extrasystoles, singly or in groups, occurred in 500 patients. Some degree of heart block was observed in 98 patients, and brief periods of tachycardia occurred in 59.

In two patients a supraventricular tachycardia developed and persisted despite withdrawal of the catheter into the vena cava. Both patients responded rapidly to orbital pressure. One developed auricular fibrillation requiring treatment with digoxin. Another patient suffered a period of breath-holding following the injection of ether for a selective ether test. He responded to a brief period of artificial ventilation with oxygen.

Fatalities occurring during catheterization are described in the section on mortality.

Post-Catheter Condition and Complications

At the termination of the study the general condition of each child was assessed as being good, fair, or poor. This assessment was based on the presence of (*a*) deterioration from the pre-catheter condition, (*b*) shock, (*c*) change in degree of cyanosis, (*d*) arrhythmia, and (*e*) vomiting. Using these criteria 625 patients were judged to be in good condition; 34 were in fair, and 11 in poor condition. Only 17 patients appeared shocked. Their condition became good following the infusion of small volumes of whole blood (Table II).

TABLE II

Condition at Termination of Study

Condition	Before transfusion	Number transfused	After transfusion	
Good	625		642	95.8%
Fair	34	16	18	2.7%
Poor	11	1	10	1.5%

In 262 patients a selective angio-cardiogram was performed as the last step of the catheter study. Nine patients in otherwise good condition suffered complications following this procedure. Tachycardia occurred in two patients. Cyanosis deepened in two patients and apnoea occurred in another two. All four children responded quickly to the administration of Coramine. Three patients vomited following the injection of the contrast media.

On return to the ward the majority of patients slept for several hours unless aroused. They were able to take fluids when awakened, but would then fall asleep again if left undisturbed.

Fatalities occurring in the post-catheter period are described in the next section.

Mortality

Of the 670 subjects who received CM_3 4 died at or shortly after cardiac catheterization. All were given the full dose of the mixture calculated on a weight basis prior to the study.

The only death directly attributable to the mixture was that of a gravely ill cyanotic infant aged two months who was in heart failure from a true truncus arteriosus. She developed gasping respirations one hour after the administration of the mixture. Despite her poor condition a rapid study was planned. Bradycardia developed when the catheter entered the right heart whereupon the study was abandoned. The infant died twenty minutes after returning to the ward. In retrospect, this infant should not have received the full dose of CM_3, and Nalline might have revived her temporarily.

The other patients were all well sedated. One infant aged nine days with severe simple pulmonary stenosis died from the inadvertent injection of the contrast media through a catheter wedged in the coronary sinus.

Another infant aged two months with idiopathic hypertrophy of the left ventricle developed bradycardia leading to a fatal arrest during the study.

The fourth death was that of an infant aged seven months with severe simple pulmonary stenosis whose catheterization was complicated by a paroxysm of supraventricular tachycardia. This was terminated promptly by pressure on the eyeball. The infant was returned to the ward in good condition, appeared well an hour and a half after the study, but was found dead in her crib one hour later.

Two other patients are of interest. One was a seven-day-old infant who was catheterized without preliminary sedation because of poor general condition. Restlessness developed just as the catheter was passed through an interventricular defect into the root of the aorta. A diluted mixture of 0.04 cc. CM_3 in saline was then injected through the catheter. Cardiac arrest occurred immediately. Massage was instituted within two minutes and normal cardiac activity returned within fourteen minutes. The infant recovered completely, but died two weeks later at the time of open heart surgery.

One eleven-year-old boy with a complex malformation producing marked cyanosis underwent a study lasting two hours without incident under CM_3 sedation. A few days later a catheter was inserted again, but this time without sedation for the purpose of carrying out a selective angio-cardiogram. Fatal arrhythmias developed when the catheter reached the right atrium.

Discussion

Where general anaesthesia is not used for cardiac catheterization of infants, and children, different methods of sedation for maintaining a steady state have been employed. Inadequate sedation with resulting restlessness and crying is the chief problem encountered. The use of CM_3 by intramuscular injection has almost completely overcome this problem. Since individual tolerance to the mixture varies, employing an arbitrary schedule of dosage will result in a certain number of patients being over-sedated while others will require additional amounts of the drug to achieve satisfactory sedation. In view of this variation the safest method of sedation is (*a*) to deliberately under-sedate initially, and (*b*) to supplement with small increments of the mixture via the catheter.

The mixture can provide optimum conditions for cardiac catheterization in all patients in the younger age group providing that certain important precautions are observed. Firstly, in cyanotic infants or infants in grave condition the initial dose should be reduced by 20–50 per cent of the arbitrary dose depending on the degree of cyanosis and debility. Secondly, should supplementation become necessary, any addition quantity of CM_3 should be given slowly in dilute solution through a catheter situated no further centrally than a vena cava.

The mixture has also been used as sedation for 203 patients undergoing venous angiograms, 13 undergoing hepatic wedge pressure determinations, and for a few receiving EEG investigations. While the data for these patients is not presented, the effectiveness of the sedation has satisfactorily paralleled the results in the catheter series reported above.

Summary

A mixture of chlorpromazine, promethazine and Demerol was administered intramuscularly as sedation to 670 children undergoing cardiac catheterization.

With certain modifications, an arbitrary dosage schedule of 1 cc./20 lb. was employed. Infants in poor condition or with cyanosis received 50–80 per cent of this arbitrary dose. A maximum dose of 1.5 cc. was used in patients weighing more than 30 pounds. Those patients who were insufficiently sedated were supplemented with small diluted quantities of the mixture given via the catheter. Such injections should be made into a vena cava rather than into a chamber of the heart.

Details of four deaths occurring in the per-catheter and post-catheter periods are presented.

Acknowledgment

The authors are indebted to Dr. J. D. Keith, Chief Cardiologist, Hospital for Sick Children, Toronto, in whose department the catheter studies were performed.

Résumé

Pour permettre de leur faire un cathétérisme cardiaque, on a donné à 670 malades dont l'âge variait de 4 jours à 16 ans, un mélange de chlorpromazine, du chlorhydrate de promethazine et du Demerol. Ce mélange (une partie de chlorhydrate de promethazine et une partie de chlorpromazine avec 2 parties de Demerol) a été donné en injection intramusculaire à raison de 1 ml. par 20 livres de poids sans toutefois dépasser 2 ml. Chez 26 malades, après l'introduction du cathéter, on a donné des doses fractionnées par voie endoveineuse. Avant le cathétérisme, l'état des malades était bon chez 31.9% des cas, passable chez 54.6% et mauvais chez 13.5%. Chez 97.3% des cas, cette sédation a été adéquate et elle ne l'a pas été dans un pourcentage de 2.7%. Au delà de 70% de ces examens ont duré de une heure à deux heures. A la fin de l'examen, 95.8% des malades étaient en bon état. Les arythmies les plus fréquemment observées furent des extra-systoles, des blocages nerveux et de la tachycardie paroxystique.

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AN APPRAISAL OF THE PRESENT TREATMENT OF BARBITURATE POISONING[1]

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THE IMPORTANCE OF BARBITURATE POISONING AS A THERAPEUTIC PROBLEM

The greatly increased importance of acute barbiturate poisoning as a therapeutic problem is forcefully documented (1) by recent statistics from Britain (2, 3), the Scandinavian countries (4, 5), and the United States (6, 7). The annual consumption of barbiturates in the United States is 300 tons. The increasing popularity of barbiturates as suicidal agents has created a world-wide problem. The incidence of suicide by means of barbiturates is approximately 5 per cent of that for all poisons and in large cities this figure may be fourfold. About 20 per cent of hospital admissions for acute drug intoxication are cases of barbiturate poisoning; only carbon monoxide poisoning exceeds this figure. About 1,500 deaths from acute barbiturate intoxication occur annually in the United States alone. When one takes into account the discrepancy between reported and actual number of deaths, as well as the probable ratio of 13 to 1 of reported non-fatal cases to fatal cases, some perspective is gained in assessing the magnitude of the problem.

A SUMMARY OF THE PATHOLOGIC PHYSIOLOGY OF ACUTE BARBITURATE POISONING

Definition of Barbiturate Poisoning

Barbiturate poisoning refers to the physiological and psychological changes produced by a toxic amount of any member of this class of drugs (6, 7).

Moderately severe poisoning usually occurs when an amount of barbiturate has been ingested which is five to ten times the full oral hypnotic dose. The *fatal dose* varies with many factors, as will be noted later, and cannot be stated with certainty, but when over fifteen to twenty times the ordinary hypnotic dose has been absorbed, severe poisoning will ensue (7) and even expert therapy may fail to save the patient's life.

Aetiological Factors in Acute Barbiturate Poisoning

There are three main factors. Poisoning by barbiturate may occur in three ways. (i) *Accidentally*, in the course of its therapeutic use, when given intravenously for anaesthesia by persons not sufficiently experienced in this field, and rarely idiosyncrasy may be the basis of intoxication. (ii) ***Suicidal intent*** has its modes and the use of barbiturates is currently in vogue. There is usually some psychiatric disorder, most commonly in the reactive depressions, manic-depres-

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sives and schizophrenics. (iii) Occasionally, acute barbiturate poisoning may be due to what has been called "automatism." For example, failure of the drug to produce sleep may cause a confusional state in which the patient does not remember having already taken medication and he may then unwittingly ingest an overdose (6).

Toxicological Factors in Acute Barbiturate Poisoning

(*a*) *Central nervous system.* The major action of the barbiturates is depression of the central nervous system. The intensity of this effect depends upon (i) the particular barbiturate ingested, which will govern its subsequent *in vivo* metabolism, distribution and excretion; (ii) the dose; (iii) the clinical status of the patient, such as age, sex, weight, and reflex irritability; (iv) environmental factors (8), such as temperature, barometric pressure and humidity. Evidence seems to indicate that the barbiturates act at all segmental levels and at all levels of functional organization of the central nervous system. Although the finer mechanism of action is not yet fully elucidated, nevertheless two properties of barbiturates have been established beyond question (9, 10). There is an elevation of the threshold of stimulation of neurons by stabilization of the cell membrane (9) and prolongation of the time for recovery from excitation. The neurons of the cerebral cortex, the reticular activating systems of the mid-brain and diencephalon are most susceptible to depression by the barbiturates (10). Internuncial neurons are more susceptible than neurons which directly subserve reflex arcs. The cerebellar, vestibular and spinal systems are less sensitive and the vital medullary systems concerned with respiration and circulation are least sensitive. Thus, barbiturates first depress the cells of the reticular activating system and the cerebral cortex. These actions lead to difficulty in thinking, impairment of judgment and finally to sleep. As the degree of intoxication increases, the activity of the cortical and reticular cells is further depressed, the cerebellar and vestibular systems become involved, and depression of spinal cord activity appears. The results are increasing impairment in mental ability, confusion, light coma, ataxia, and depression of deep tendon reflexes. As the intoxication deepens, coma becomes complete and the deep reflexes are lost (6).

(*b*) *Cardio-vascular system.* There is a central depression of the vasomotor centre with peripheral vasodilatation and hypotension. Barbiturates can also produce dilatation of the finer blood vessels by directly affecting their musculature. Excessive concentrations may dilate and injure capillary beds so that shock may ensue. The untoward effects on the cardiovascular system observed in acute barbiturate poisoning are to some extent secondary to hypoxia due to respiratory depression. However, experimentally, very large doses have been shown to produce cardiac irregularities and even cardiac failure in heart-lung preparations.

(*c*) *Respiration.* The medullary respiratory centre is depressed directly, breathing becoming slow and shallow. This is the major danger in acute barbiturate intoxication. Indeed, death from barbiturate poisoning may be due to respiratory failure, but not necessarily so. In barbiturate poisoning, the sensitivity of the respiratory centre to the normal carbon dioxide stimulus may be abolished, but the intensity of the reflex response to hypoxic chemo-receptive

impulses may not be greatly affected. Thus breathing may be largely controlled by the hypoxic drive to respiration through the carotid and aortic chemo-receptor mechanism. Reduced oxygen tensions in the blood may thus temporarily mask serious medullary depression by barbiturates. Very low oxygen tensions ultimately exert a depressant effect on the medulla, combining with barbiturate depression to cause death. This fact is important since administration of oxygen alone at this stage may remove the stimulus to respiration and cause cessation of breathing.

Clinical Aspects of Acute Barbiturate Poisoning

(*a*) *Signs and symptoms.* It will be understood from the foregoing discussion, that the signs and symptoms are referable especially to the central nervous, cardiovascular, and respiratory systems. They vary with the amount and type of drug used, the length of time since it was ingested, and duration of time without treatment. In general (6), the larger the dose the more rapidly signs and symptoms appear and the longer they persist, regardless of the drug used. Pentobarbital and secobarbital produce coma quickly but recovery is relatively rapid. Barbital and phenobarbital slowly induce coma which is prolonged. These differences are due to variations in the speed of the detoxification of the different barbiturates. Cases of acute barbiturate intoxication may be classified as mild, moderate or severe, according to the degree of depression of the central nervous system. Differentiation of these various grades is very important in planning treatment and assessing the results (11, 12).

(i) *Mild intoxication.* The patient is not comatose and is easily aroused by mild stimulation. There is impairment of mental ability, judgment and emotional stability. Neurological signs include transient nystagmus on lateral gaze, dysarthria, ataxia in gait and station, adiodokokinesis, and depression of the superficial skin reflexes.

(ii) *Moderate intoxication.* The patient is comatose but can be aroused by very vigorous manual stimulation or by the intravenous injection of 5 ml. of a 10 per cent solution of metrazol. Respiration is slow but not shallow, and cyanosis is not present. Nystagmus is constant. The patient when awakened cannot stand or walk alone because of ataxia. The deep tendon, corneal, and gag reflexes are depressed but not absent. Patients with mild or moderate barbiturate poisoning almost always recover.

(iii) *Severe barbiturate intoxication.* The patient is comatose and cannot be aroused by manual stimulation or by metrazol (11). Respiration is slow, shallow, and cyanosis is frequently observed. There is often Cheyne-Stokes rhythm and pulmonary oedema may be present. The deep tendon reflexes are markedly depressed and may be unobtainable. A Babinski response is often elicited. Corneal and gag reflexes may be absent. The pupils may be constricted and unreactive to light; if anoxia is severe, they may be dilated. The pulse is rapid and thready. The blood pressure may fall to shock levels. Unless the patient has developed bronchopneumonia, the body temperature is 0.5° to 2.0°C. below normal. Urine formation is decreased or suppressed. This fact is of therapeutic importance because the longer-acting barbiturates cannot be adequately detoxified in the tissues and recovery from their effects is dependent upon adequate renal function.

(*b*) *Diagnosis.* The diagnosis is made from a careful evaluation of a history from friends, relatives and police officers, the physical findings and by identifying barbiturate (13) in stomach contents, blood or urine. Of course, acute barbiturate poisoning must be differentiated from all other conditions which cause coma: for example, head injuries, cerebro-vascular accidents, brain tumours, meningitis, encephalitis, diabetic and uraemic coma, syncope due to cardiovascular causes, hepatic coma and coma due to other intoxicants; alcohol, morphine, bromide and other aliphatic hypnotics.

(*c*) *Assessment* of severity, progress of intoxication and response to treatment is best made by keeping an accurate chart of the status of the important vital functions and reflexes every 15 to 30 minutes. By following such a chart, one can quickly detect the deceptive simulation of deep barbiturate coma by the secondary effects of hypoxia; simple correction of hypoxia rapidly leads to improvement in vital signs.

(*d*) *Complications.* The most common complications of acute barbiturate intoxication are pulmonary (6). Death, if it occurs, is usually the result of paralysis of the respiratory centre. The shorter-acting barbiturates are particularly liable to produce death from respiratory depression (7). If death is delayed, vasomotor collapse, cerebral oedema and hypostatic pneumonia are the usual causes. Bronchopneumonia, lung abscess, or other pulmonary complication may occur in a patient who has regained consciousness and apparently recovered. Hyperthermia and lower nephron nephrosis are also serious complications. Decubitus ulcers may develop (6). It is not unusual for acute barbiturate intoxication to be superimposed on barbiturate addiction, and if this is true, severe withdrawal signs may appear, after the patient has recovered from coma.

There are no characteristic autopsy findings, although diffuse, non-specific cerebral lesions may occur (7).

(*e*) *Prognosis* depends on the amount of drug taken, the particular barbiturate used, the general health of the individual, the interval elapsing between the ingestion of the poison and the beginning of treatment and the nature of the therapy.

Apparently, hyperaemia of the gastric mucosa caused by a strongly alkaline sodium barbiturate facilitates direct and rapid absorption from the stomach. The onset of coma is so rapid that barbiturate intoxication is often not suspected by the physician (6).

Therapeutic Management of Acute Barbiturate Poisoning

The objectives of therapy are: (i) to prevent in so far as possible further absorption from the intestine, (ii) to support the respiration and blood pressure, (iii) to decrease the intensity of depression, and (iv) to prevent complications.

There is a general tendency to over-treat the patient poisoned by central depressants. In cases of mild to moderate intoxication, little therapy other than supportive measures may be required. The patient may be better off if allowed to recover unaided by strong analeptics than if he is the recipient of well-intentioned but ill-designed treatment (4, 5, 7).

Supportive and Expectant Therapy

This approach to the management of acute barbiturate poisoning is advocated by all groups and particularly by Clemmesen (5) and Nilsson (4). The importance of (i) adequate oxygenation, and (ii) respiratory exchange (endotracheal intubation indicated if pharyngeal and larygeal reflexes absent), (iii) toilet of the pharyngobronchial tree, and (iv) use of pressor agents for vascular hypotension and wide spectrum antibiotics, cannot be stressed too heavily, as the basis of any therapeutic programme. Using these principles in the management of acute barbiturate poisoning the results of Clemmesen's group (5) in Denmark are indeed impressive. Over the past six years they have reduced the mortality rate from barbiturate poisoning in Denmark from 25 per cent to 3.7 per cent and even down to 1.6 per cent in Copenhagen, despite an increase in the number of cases admitted to Danish hospitals, which have more than doubled over this period.

Chemical Antidotes

(*a*) *Central analeptic drugs.* Present-day therapeutic controversy, in the management of acute barbiturate poisoning, centres about the use of analeptic drugs, particularly picrotoxin and pentylenetetrazol (metrazol). The range of published opinion includes enthusiasm (12, 14); cautious acceptance (15); ambivalence (16), and condemnation (4, 5).

The analeptic drugs have been used to stimulate the depressed respiratory centre and lessen the degree of central depression by excitation of higher centres. Caffeine and sodium benzoate, and Nikethamide (coramine) have been used, but their value is questionable (17). The use of strychnine has fallen from favour (7). Sympathomimetic amines with a relatively strong central stimulant action and weak peripheral sympathetic effect have been employed. That is, amphetamine (benzedrine), d-amphetamine (dexedrine), and desoxyphedrine (methedrine) are viewed by some as the agents of choice (7). Others prefer metrozol or picrotoxin (12, 14). Combinations of analeptics are often of more value than a single agent, and such combinations as picrotoxin and amphetamine and picrotoxin and metrazol (6) have been used.

In the evaluation of individual analeptic agents Eckenhoff (15) points out that three facts must be recognized: (i) patients have recovered from more than the usual fatal dose of barbiturate without aid of analeptics; (ii) definite hazards exist in the use of analeptics; (iii) no analeptic, as yet, can be depended on to cause the recovery of a patient deeply depressed from a usually fatal dose of a barbiturate. Further, it is difficult to obtain significant data owing to (i) a wide variability in human and animal response to barbiturate; (ii) great variety of M.L.D.; (iii) different degrees of absorption; (iv) presence of co-existent disease; (v) age; (vi) physical state; (vii) great variability in the period between treatment. Nevertheless, each central stimulant has its ardent advocates who present clinical data purporting to show the superiority of their particular analeptic, but unfortunately often fail to clearly indicate the variables involved in their series.

The case against analeptics has been forcefully presented by Nilsson (4) and

Clemmesen (5). Nilsson treated 176 cases by conservative (supportive expectant) measures alone, with a fatality rate of only 1.7 per cent; even in the group of 87 severely poisoned patients the death rate was only 3.45 per cent. These results are better than those in most reports of adequately large series of cases treated with analeptics.

The case for analeptic therapy is well campioned by Kappanyi and Fazekas (11, 12), who regret Nilsson's pharmacotherapeutic nihilism, admit that not all patients require central stimulant therapy, but emphasize the value of analeptics in properly selected cases. They propose that differentiation can be made between those not requiring analeptics and those requiring vigorous therapy with picrotoxin and metrazol by the results of the intravenous injection of an orientation dose, 5 ml. of a 10 per cent metrazol solution. If twitching and grimacing occur and the corneal and deep tendon reflexes return, only symptomatic care is indicated and analeptics need not be used.

The action of metrazol is prompt and brief, so that the effects are more readily controlled than those of pictrotoxin which are sometimes delayed for as long as ten minutes, even after intravenous injection, a fact which complicates its clinical use.

Since picrotoxin was first introduced for the therapy of acute barbiturate poisoning by Arnett (18) in 1933, there have been numerous reports of dramatic and life-saving results from its use. When properly administered, picrotoxin is unequaled for its long-sustained stimulatory effects. By acting on the medulla and brain-stem, it improves respiration and circulation, hastens the return of swallowing and cough reflexes, and induces restlessness and movement which prevent dangerous circulatory stasis. Metrazol though more transitory in its action than picrotoxin is more effective on higher cerebral centres.

The dose and route of administration of picrotoxin depend upon the urgency of the case. In seriously poisoned patients in coma, the drug is given intravenously by one of two methods. *Method I*: a continuous infusion at the rate of 1 or 2 mg./min. until the corneal and swallowing reflexes appear or until very slight twitchings of the facial muscles or extremities occur; then give intramuscularly in doses of 3 to 6 mg. every 15 to 30 minutes depending on the course of recovery and response. *Method II*: fractional method by which 6 to 12 mg. (2 to 4 ml. 0.3 per cent solution), are given intravenously every 10 to 20 minutes.

There are serious dangers with picrotoxin that should be realized. Because it has a long latent time of action, an injection of picrotoxin should not be repeated until the previous dose has manifested its full effect, which may require ten to twenty minutes or longer. Complications with picrotoxin arise from the fact that if the clinician does not wait this full interval (which unfortunately is so often the case), convulsions are most likely to ensue. This leads to secondary depression of a postictal type and from the subsequent barbiturate which is administered to control the convulsions. Thus a vicious circle is begun.

The administration of these potent analeptic drugs necessitates careful and close observation of the patient, and good judgment in the selection of doses and intervals between doses.

If metrazol is employed, it is given intravenously in amounts of 3 to 5 ml. of a 10 per cent solution every 5 min. for 2 or 3 doses, as required.

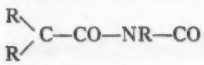
The objective in analeptic therapy is to restore and continuously maintain active reflexes, spontaneous involuntary movement, and responsiveness to pain, until sufficient barbiturate is eliminated to ensure recovery and yet not produce convulsive twitchings from an overdose. One does not attempt to restore the patients to full consciousness by drug therapy. Indeed, this is an impossibility and convulsions will occur if such an attempt is made.

(*b*) *Sodium succinate and related compounds.* From experiments based on the observation made by Quastel and Wheatley (19) that barbiturates inhibit the utilization of glucose, lactate and pyruvate but not of succinate by brain tissue *in vitro*, Soskin and Taubenhaus (20) reported that succinate was an effective antidote against pentobarbital. This report initiated a number of investigations in animals (21–27), and in man to determine whether certain dicarboxylic acids (succinic, fumaric, malonic (28), pyruvic (25)) could shorten the duration or decrease the intensity of barbiturate depression. Although the use of disodium succinate has its advocates, they are few (27), the consensus being that this approach to antidotal therapy has not as yet yielded acceptable evidence of benefit.

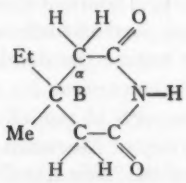
Because of the failure of succinate and of the dangerous reactions accompanying overdosage with central analeptics there have been a continuing constant search for a chemical antidote which might effectively, without producing convulsions, reverse barbiturate depression by specific antagonism. Along this line, recent compounds introduced are those mentioned below.

(*c*) *B-B-ethyl methyl glutarimide* (*Megimide; NP$_{13}$; Bemegride*) *and 2-4-diamino-5-phenylthiazole (D.A.P.T.).* (i) *History.* B-B-ethyl methyl glutarimide was first synthesized in 1911. Shaw first observed its anti-barbiturate activity in 1951 and subsequently investigated it in animals (29) and in man (30) in 1955.

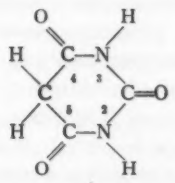
(ii) *Chemistry and pharmacology: Megimide.* Marshall *et al.* (31) point out that there is a similarity between part of the structure of Megimide and barbiturates, the grouping



being common to both.



B-B-ETHYL METHYL GLUTARIMIDE (MEGIMIDE)



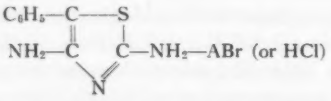
BARBITURIC ACID

Because of this the hypothesis was advanced that probably the similarity of structure enables the glutarimide, when offered in sufficient concentration, to displace the barbiturate molecules from the receptors to which they are attached and so to reduce their effect, that is, competitive inhibition. Megimide is more

active than D.A.P.T. Recently, Cass (32) studied electro-encephalographic patterns of the analeptic action of B-B-ethyl methyl glutarimide in rabbits against pentobarbitone, thiopentone, amylobarbitone, Thialbarbitone and other hypnotics such as chlorolon, ether and oblivon. Megimide reversed the EEG changes induced by pentobarbitone, thiopentone, amylobarbitone and Thialbarbitone, but produced only minimal improvement, if any, in animals depressed by non-barbiturate hypnotics (chlorolon, ether, oblivon). In the basis of EEG patterns Megimide was found to be a more effective barbiturate antagonist than coramine, methedrine, picrotoxin and leptozol.

Although the biophysical processes resulting in the electrical changes shown in these EEG's are not fully known, the assumption is made that a drug which restores an electrical pattern similar to that of light anaesthesia is antagonizing the anaesthetic used. Evidence does not suggest any particular type of antagonism although Megimide only antagonizes barbiturates. Regardless of its mode of action, as a stimulant it has novel features. It does not raise the blood pressure or induce hyperpyrexia as do analeptics, and it does not seem to provoke increased oxygen consumption by the cerebral tissue.

Because it may cause convulsions in large doses, Shulman *et al.* (30) proposed a second substance *D.A.P.T. (2-4-diamino-5-phenylthiazole)* be used in conjunction with it. It is itself a weak barbiturate antagonist, a good synergist to NP_{13} as well as an excellent respiratory stimulant (30, 33).



It is claimed to greatly reduce the risk of toxic manifestations which sometimes occur when NP_{13} alone is given rapidly and in high dosage.

Shaw *et al.* (29) have indicated that both these substances possess a high therapeutic index.

(iii) *Advantages claimed.* Because of favourable results in recent clinical trials (29, 30, 33, 34, 35), showing restoration of the patient from a deep coma to a desired state of light anaesthesia—"the safe state"—from which spontaneous recovery to full consciousness usually occurs within eight hours; it thus removes the need for strict, prolonged medical and nursing care, and virtually eliminates the risk of complications, and will eventually further reduce the death rate.

(iv) *Mode of administration.* Have 2.5 per cent thiopentone Na at hand. Give intravenously every 3 to 5 min. 1 ml. of a solution with 15 mg. of amiphenozole followed at once by 10 ml. of a solution with 50 mg. of Megimide. This is continued until the patient is restored to what is called the "safe state," that is, when pharyngeal, laryngeal reflexes return, blood pressure, heart rate and respiration approach normal. Usually two hours of treatment in a deeply comatose patient is adequate. On an average 1 gm. of Megimide and 0.3 gm. of D.A.P.T., is required, though the amounts may vary with the depth of the intoxication.

(v) *Complications.* Vomiting or retching are usually the earliest and may be the only clinical signs of incipient toxicity. This may be followed by slight

flickering of the fingers and is readily reversed by small amounts of intravenous 2.5 per cent thiopentone (30). Regression may occur and further small treatments are indicated. This is more likely to occur when coma has been of long duration before therapy began, or if a long-acting barbiturate is involved. Lauw and Sonne (35) have observed mild, short-lived attacks of tonic-clonic convulsions. Psychic disturbances have been reported recently following Megimide therapy (35, 36). They occurred mainly in addicts to barbiturates, but also in non-addicts.

(vi) *Present status.* Megimide and D.A.P.T. have a striking stimulating effect on reflex activity as well as on respiration, and they are valuable for bringing patients into a stabilized physiological state, the so-called "safe state" (35). On the other hand, in several recent series of clinical experiences (33–37) it was found that in severe cases the drug did not influence the rate at which barbituric acid was eliminated, the blood level of barbituric acid on waking, or the duration of coma. The majority of workers do not support the hypothesis that Megimide is an antagonist in a strictly biochemical sense (like, for example, nalorphine in morphine poisoning). It seems that the drug counteracts barbituric acid by a central stimulant action. This is indicated by the reflex hyperactivity, the EEG changes, and the complications caused by an overdose, which are not readily compatible with the assumption of a simple biochemical antagonistic effect, as, for example, competitive inhibition. Most feel that if only because of their effect on respiratory paralysis they are valuable adjuvants in the treatment of acute barbituric acid poisoning (33).

Removal of the Barbiturate from the Body

Unfortunately, none of these previously mentioned measures may be sufficient in the severely poisoned patient and in the absence of a well-established chemical antidote. The most direct approach to the management of acute barbiturate poisoning is the removal of the drug from the body. Several ways of effecting this were tried.

(i) *Gastric lavage*; (ii) *induction of diuresis.* These methods are limited in efficacy and carry potential dangers. Patients are frequently seen too late for effective lavage and it is a procedure which markedly increases the danger of aspiration. The value of diuresis is limited by the metabolic and renal excretion patterns of most barbiturates, particularly the short-acting ones.

(iii) *Peritoneal lavage* is not successful in dogs in shortening recovery period (41).

(iv) *Haemodialysis.* In the past three years, considerable experimental (38, 39, 42) and clinical data (1, 39, 40, 43) have accumulated on haemodialysis as an efficient method of barbiturate removal. Barbiturate molecules can be mobilized from tissue and made to pass into the blood stream and then through a cellophane membrane into a dialyzing solution.

An excellent recent report by Berman (1) of eight cases of severe barbiturate poisoning treated successfully by haemodialysis, the largest series of patients treated in this manner to date, is of some significance. One of these patients, a 28-year-old, 83-lb. epileptic, is of particular interest. She had ingested 25 gm. of

phenobarbital, and did not respond to metrazol, picrotoxin, caffeine or sodium benzoate therapy. When seen by Berman's group 49 hours after ingestion of the drug, she was comatose, areflexic. Her initial blood barbiturate level was 25.3 mg./100 ml.

After three dialyses, 9.33 gm. of phenobarbital were recovered, representing 37 per cent of the ingested dose, a figure in good agreement with the experimental dialysis of phenobarbital (38). This indirectly corroborated the patient's statement concerning the amount of drug ingested, a statement otherwise difficult to believe. Following the dialyses return to consciousness was rapid and complete.

The efficiency of haemodialysis in removing barbiturate varies directly with the concentration gradient from blood to bath; therefore, the higher the blood level of barbiturate, the faster its removal by haemodialysis will be. Also, the amount of drug which can be removed increases with the severity of poisoning, a unique feature for any therapeutic procedure.

Other variables are the surface area of the cellophane which is relatively constant, but flow rates through the machine are influenced by cannula size, cardiac output, mean arterial pressure, all of which are difficult to maintain at maximally efficient conditions. In practice this means that patients who are initially in poor condition and who improve as dialysis proceeds, simultaneously improve the rate of extraction of barbiturate from their blood and tissues. Thus dialysis improves both the patient's condition and its own efficiency as the treatment proceeds. It has been indicated (44) that the dialysis technique is complex, requiring highly trained personnel, close supervision and is not without hazards of its own. However, results such as Berman's (1) suggest that it may come to have an important place in the treatment of severe barbiturate poisoning.

Physical Method of Stimulation

Electro-stimulation (non-convulsive). Robie (45) has claimed that non-convulsive electro-stimulation (of temporal areas) lessens barbiturate depression and favourably influences respiration. He advocated the use of unidirectional electro-cerebral stimulation. A modulated current of 5 to 7 milliamperes is applied through electrodes fastened to the temples. According to Robie, the application of the current immediately increases the depth of respiration, and the effect on respiration can be varied by altering the modulation and amount of the current. Duration of stimulation is usually 1½ to 5 hours, whereupon the patient can be awakened. The mechanism of the response had been explained as a result of the activation of cortical or diencephalic structures. However, this does not appear to be altogether true since Blackly (46) was able to get similar respiratory responses when the electrodes were applied peripherally (on the medial aspect of middle part of each lower leg). Thus it is now believed that respiratory augmentation resulting from electro-stimulation is a reflex mechanism dependent on the excitation of general somatic afferent nerve fibres. Blackly feels that peripheral stimulation is preferable to bitemporal, since respiratory inhibition which sometimes occurs with bitemporal stimulation is less likely to occur in the peripheral method. He failed to indicate that stimulated dogs awakened earlier

than control animals. This method of management requires further confirmation from experiments on human beings.

Comments and Conclusions

(*a*) The science of human toxicology is continually beset by problems relating to minimum lethal doses, fatal blood levels of drugs, and effectiveness of treatment, inasmuch as there can never be a sizable body of data wherein the pertinent variables are well controlled. For example, in a clinical series of patients with acute barbiturate poisoning, factors such as inaccurate history of dosage, ratio of ingested dose to absorbed dose, time elapsed before treatment, underlying physical state (for example, renal function, visceral pathological changes in the kidney and liver), and individual variation in tolerance to drug may make it difficult to assert that any given patient would have survived with or without a particular therapeutic procedure.

(*b*) The world-wide prominence of acute barbiturate poisoning is a stimulus for continuing improvements in therapy.

(*c*) A comprehensive understanding of the pathological physiology of acute barbiturate poisoning is an essential prerequisite to intelligent therapy.

(*d*) The initial assessment of severity, progress of intoxication and response to therapy are all important guides in the choice of subsequent management of patients with acute barbiturate poisoning.

(*e*) All groups agree as to the benefits and helpfulness of supportive expectant therapy. The present-day controversy centres on the use of central analeptics of which picrotoxin and metrazol are most commonly employed either separately or conjointly. Their use is not without dangers. They are not always effective in severe barbiturate poisoning.

(*f*) The consensus of opinion is that sodium succinate is not useful in acute barbiturate poisoning.

(*g*) Recently, non-convulsive electro-stimulation has been advocated, but it has yet to be confirmed in human patients as being beneficial in acute barbiturate poisoning.

(*h*) Two major recent advances in the treatment of acute barbiturate poisoning are: (i) the use of Megimide and D.A.P.T. as chemical antidotes. Initially, they were believed to be true chemical antagonists to barbiturates on the basis of their structural similarity. However, it now appears that they are central analeptics but with a high specificity to barbiturates. They are by no means ideal since toxicity occurs in overdosage.

(ii) Haemodialysis, a very rational approach to the treatment of acute barbiturate poisoning, has shown very encouraging clinical results in the treatment of severe barbiturate poisoning. Unfortunately it is a rather complex technique as it exists today.

Résumé

La fréquence fortement croissante des empoisonnements aux barbituriques pose un problème thérapeutique dont la documentation est abondante d'après

les statistiques faites en Grande-Bretagne, dans les pays scandinaves et aux Etats-Unis. Aujourd'hui, ces médicaments sont devenus la principale cause de l'intoxication médicamenteuse aiguë dans le monde.

Cette expansion universelle des empoisonnements aigus par les barbituriques est devenue un stimulant pour essayer d'améliorer les traitements à prescrire.

Pour instituer une thérapeutique intelligente, il est essentiel de connaître au préalable la physiopathologie de l'empoisonnement aigu aux barbituriques. Le tableau clinique initial de la gravité de l'intoxication, de son aggravation et de la réponse du malade à la thérapeutique sont des facteurs importants pour aider à faire le choix des traitements ultérieurs dans l'empoisonnement aigu par les barbituriques.

Les objectifs de cette thérapeutique sont: (*a*) prévenir, autant que possible, une absorption plus considérable du médicament par l'intestin; (*b*) maintenir les échanges respiratoires et la tension artérielle; (*c*) corriger la dépression; (*d*) prévenir les complications.

Il existe une tendance générale à donner trop de médicaments au malade empoisonné par des dépresseurs centraux. Dans les cas d'intoxication légère et modérée, il peut y avoir peu à faire à part les mesures stimulantes. Le malade pourra peut-être en sortir mieux si on le laisse revenir seul sans administrer d'analeptiques puissants que si l'on institue un traitement bien intentionné mais susceptible de le rendre malade.

Tous sont d'accord sur les bienfaits et l'utilité de la thérapeutique de support, soit: une oxygénation adéquate et des échanges respiratoires convenables (intubation endotrachéale si les réflexes pharyngés et laryngés sont absents) la vidange de l'arbre pharyngobronchique, l'emploi de vasopresseurs pour corriger l'hypotension et des antibiotiques à puissance étendue.

Aujourd'hui, la controverse réside dans l'emploi des analeptiques centraux dont la picrotoxine et le metrazol sont les plus fréquémment employés soit ensemble, soit séparément. On ne les emploie pas sans danger. Ils ne sont pas toujours efficaces dans l'empoisonnement avec les barbituriques.

Tous sont d'accord pour affirmer que le succinate de sodium n'est pas utile dans ces cas.

On a préconisé, récemment, une électrostimulation non convulsivante mais il n'est pas confirmé que, chez l'humain, elle serait utile dans l'intoxication aiguë par les barbituriques.

Les deux principales acquisitions récentes dans le traitement de ces intoxications aiguës sont:

(*a*) L'emploi du Megimide (B-B-ethyl methyl glutarimide) et du D.A.P.T. (2-4-diamino-5-phenylthiazole) comme antidotes chimiques. Au début, on croyait qu'ils avaient un réel pouvoir chimique antagoniste aux barbituriques en se basant sur leur similarité de structure. Toutefois, maintenant, il semble bien qu'ils sont des analeptiques centraux mais possédant une haute spécificité pour les barbituriques. De toute façon, ils ne constituent pas le traitement idéal puisque leur surdosage devient toxique.

(*b*) L'hémodialyse qui semble un abord très rationnel de l'intoxication aiguë par les barbituriques a donné des résultats cliniques très encourageants dans

ces cas. Malheureusement, telle qu'elle se pratique aujourd'hui, elle requiert une technique complexe.

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EPIDURAL AND NERVE BLOCK ANAESTHESIA WITH SYMPOCAINE[1]

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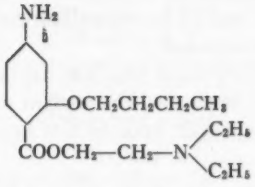
NO KNOWN LOCAL ANAESTHETIC AGENT can be said to be ideal, but we have at hand a number of reliable agents which under average clinical conditions give adequate anaesthesia with a sufficient degree of safety. The pharmaceutical houses continue to present us with new substances in the hope that the nebulous ideal may be more nearly approached. A number of 2-alkoxy derivatives of procaine have been synthesized and investigated in animals. One of these is the 2-butoxy derivative first synthesized by Clinton and Salvador (1). Its structure is:



2-DIETHYLAMINOETHYL-4-AMINO-2-BUTOXYBENZOIC ACID

Luduena and Hoppe (2) studied the drug in animals with the following results. Compared with tetracaine, Sympocaine® (WIN3706) is 1.7 times more potent in producing threshold anaesthesia in the sciatic nerve of guinea pigs and 2.3 times more potent in producing threshold anaesthesia in rabbit corneas. It reaches its threshold irritant concentration (Trypan blue intradermal test) at one-third that of tetracaine. When it is injected intravenously the acute toxicity LD50 in mice (4.0 mg./kg.) is 2.3 times tetracaine, with values of 2.3 and 2.8 mg./kg. in rabbits and guinea pigs respectively. Subcutaneously, the LD50 in mice was about the same as tetracaine and one-fifteenth that of procaine.

From these data, it was assumed that Sympocaine was one and a half times as potent and as toxic as tetracaine. In man one could then use two-thirds the clinical dose of tetracaine as a guide, although the manufacturers suggested 15 mg. as the maximum dose. Moore (3) suggests a maximum dose of 80 cc. of 0.25 per cent tetracaine and Dodd (4) suggests 40–50 cc. of 0.1 per cent for nerve block but 200–300 cc. when used for infiltration. Hewer (5) quoting James (6) suggests 2 mg./lb. with a maximum of 300 mg. Using these standards 1.3 mg./lb. or 200 mg. of Sympcaine might be considered the maximum dose. We would like to suggest from our studies that 1 mg./lb. be considered an optimal dose.

Authority	*Maximum dose*	*Comment*
Moore	80 cc. of 0.25% or 200 mg.	
Dodd	50 cc. of 0.1% or 50 mg.	Nerve block
	300 cc. of 0.1% or 300 mg.	Infiltration
Hewer	2 mg./lb. body wt. or 300 mg.	

[1]Presented at the Annual Meeting, Canadian Anaesthetists' Society, Saskatoon, Saskatchewan, June 24–26, 1957.

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Method

In view of the suggested maximum dose of 15 mg., the initial concentration used was 0.1 per cent. This proved to be inadequate and so the concentration was increased until, by trial and error, the minimum effective concentration of 0.5 per cent was discovered. Sympocaine was then used without the addition of epinephrine, which would mask the characteristics of the drug. The patients were selected at random from the surgical lists and the appropriate block performed with the new agent.

Results

In all 413 patients were anaesthetized: 175 for caudal blocks; 28 for caudal with trans-sacral (sacral) blocks; 41 for epidural blocks; 98 for brachial blocks; 47 for sciatic-femoral blocks; and 24 for miscellaneous blocks (superficial cervical, sciatic alone, intercostal, paravertebral).

The largest dose given to a patient was 400 mg. and the smallest was 30 mg. The age range was 15 to 88 years and the weight range was 98 to 350 pounds. The range of duration was one-half hour to five hours. The averages are shown in Table I.

TABLE I

Block	Body wt. (lb.)	Dose		Duration (hrs.)
		Mg.	Cc.	
Caudal	164	111	22	2.0
Caudal and trans-sacral (sacral)	157	132	26	1.8
Epidural	157	97	19	1.9
Sciatic-femoral	161	172	34	2.1
Brachial	173	150	30	2.2
Miscellaneous	155	120	24	1.7

An earlier report on the use of Sympocaine in 100 caudal anaesthesias gave an average dose of 109 mg. and an average duration of 2 hours (7). Body weight was plotted against duration of anaesthesia for 30 brachial blocks using 150 mg. doses. No relationship could be defined. Dose was plotted against duration in 80 cases of caudal, sacral and epidural blocks in two age groups: 25–40 and 55–70. No relationship could be defined between dose and duration, nor could the age groups be separately defined. Age was plotted against duration at 100 mg. dose level for 32 males using caudal block. No relationship could be defined.

Complications

Failures

(*a*) In the *caudal* group there were eight (4.5 per cent) failures which could be attributed to difficulty with technique. One incomplete caudal was continued with as the operative lesion was on that side. None of the failures seemed due to poor drug action.

(*b*) In the *sacral* group one failure was due to spotty anaesthesia, while another was incomplete on one side.

(*c*) In the *epidural* group, one failure was probably due to poor technique and another was a partial failure. Two further failures occurred after an adequate dose of the drug and were suggestive of drug failure.

(*d*) There were two incomplete *brachial* blocks in which the cause for failure was uncertain.

(*e*) One *sciatic-femoral* block failed and this was almost certainly due to poor technique.

(*f*) In the miscellaneous group, one sciatic block failed due to poor technique.

Possible Evidence of Toxicity

(*a*) In the caudal group, there was one case each of: (i) generalized pilomotor response; (ii) generalized flush for one minute; (iii) drowsiness for ten minutes;

TABLE II

DETAILED LIST OF HYPOTENSIONS

Age	Sex	Weight	Operation	Dose (mg.)	Onset	Duration (hrs.)	Height	Comment
				CAUDALS				
47	F	—	Haemorrhoid	100	10	2	T12	Apprehensive 130/80 106/70; V.P.[a]
62	M	135	T.U.R.	45	4	—	T6	180/110–110/80; V.P.
31	M	145	Haemorrhoid	115	6	—	—	Very apprehensive 110/60–60/30
64	M	114	Rectal polyp removal	65	2	—	—	No unusual spread; patient prone and very flexed; V.P.
38	M	198	Haemorrhoid	125	1½	2	—	Faintness, hypotension, sweating; V.P.
64	M	190	T.U.R.	95	5½	3	—	No unusual spread 110/80–90/70. V.P.
50	F	120	Haemorrhoid	70	1	3	—	Systolic fall 190–140 with nausea
				EPIDURALS				
57	M	165	L.I.H.	110	6	2½	T8–L2	Moderate fall; V.P.
61	M	160	L.I.H.	75	4	1½	T8–S3	130/80–100/60
44	M	175	Vein stripping	100	8	—	—	Progressive hypotension, with progressive rise in level after injection
52	M	145	L.I.H.	65	6	1½	T8–S3	40 mins. after onset sudden fall 96/54–64/34; no change in level or status of patient
57	F	—	Gastrostomy	125	5	1½	—	B.P. fall; V.P.
75	M	172	R.I.H.	75	12½	2	T8–L2	Hypesthesia 2–3 segments either way; 118/78–96/56. V.P.
68	M	140	R.I.H.	85	7½	2	T3–?	130/60–90/50. V.P.
86	M	—	Strangulated I.H.	60	7½	1½	T10–L4	110/70–90/50. V.P.
33	M	161	Pilonidal cyst	100	3	2¼	—	Fall of 30 points systolic; V.P.
72	M	116	Gastrostomy	75	7	2¼	T4–?	120/80–95/60
				SACRALS				
56	M	150	Proctoscopy polyp removal	250	15	2	T12 on L S3 on R.	B.P. fall requiring V.P.

[a]V.P. = Vasopressor given with satisfactory results

(iv) failure to respond to the spoken voice for a very short period, with spontaneous recovery.

(*b*) In the sacral and epidural groups there were no cases of toxicity.

(*c*) In the brachial block group four patients became drowsy and one felt chilly (doses in mg. 150, 225, 100, 300 and 125).

(*d*) One patient who received a sciatic-femoral block in which 250 mg. were used became apprehensive and "tremulous."

(*e*) There was no evidence of toxicity in the other groups.

Hypotension

Hypotension occurred in 18 cases among the epidural-type blocks: 10 epidurals (25 per cent); 7 caudals (4.0 per cent); and 1 sacral (3.7 per cent). Hypotension did not appear in the other groups of blocks. From Table II it can be seen that the cause of hypotension in these groups was more likely related to the form of block and consequent loss of sympathetic vasomotor control.

Evidence of Irritation

Transient stinging or burning on injection occurred in the groups of blocks other than the epidural type; these latter had skin wheals of procaine. In the brachial block group, 37 out of 98 patients had these: a high incidence of about 38 per cent. No evidence has appeared suggestive of any more serious form of irritation in the skin or deeper tissues. The preservative in the solution contains among other things 1:600 phenol and this will be modified if the drug is marketed.

Dosage

Caudals

This technique was used largely for rectal and perineal surgery. The chief dose groups were 50–75 mg. (39 cases); 76–100 mg. (65 cases) and 101–125 mg. (31 cases). The common doses were 15 cc. (75 mg.) or 20 cc. (100 mg.). On occasion, even these doses may give a higher level than desired, as can be seen from the examples in Table III.

TABLE III

Examples of Excessive Spread

Age	Sex	Weight (lb.)	Dose (cc.)	Level	Operation	Comments
47	F	—	20	T12	Haemorrhoid	B.P. fall
40	M	130	15	L1	Haemorrhoid	
31	F	—	23	T11	Haemorrhoid	
54	M	193	17	L1	Haemorrhoid	
27	M	168	20	T8	Ischio-rectal abscess	B.P. fall
46	M	139	25	T3	Anal fistula	

Altogether, twenty-two (12.5 per cent) of the levels were too high; five (3 per cent) of these were excessively high, but only two could be related to generosity in dosage. It must be kept in mind that there is considerable variability in the anatomy of the region, in particular the volume, which can vary from 12 to 65 cc.

(8). Test doses of 5 cc. were used routinely and these were then followed by the main dose of a size thought to be adequate.

Epidurals

The spread in this form of block appeared to be good and an adequate 6 to 8 segment block can frequently be performed using only 15 cc. (75 mg.). Where a catheter is inserted into the space, this is suggested as the initial dose.

Brachials

The most common doses used were either 20 or 30 cc. (100 or 150 mg.). Both of these doses were effective and seemed to last about two hours; the smaller dose did not appear to be less reliable or less effective and is likely adequate for routine use.

Sciatic-Femorals

For the sciatic 20–30 cc. (100–150 mg.) were used commonly, for the femoral, 5–10 cc. (25–50 mg.) with satisfactory results.

Discussion

Despite the evidence of toxicity in animals it seems fairly certain that, when used for the variety of blocks already mentioned, a dose of 1 mg./lb. is a safe dose of Sympocaine, and that this dose is not the maximal. The complications in the doses used appear to have been very few. The hypotensive episodes are almost certainly referable to the form of block (lumbar and caudal epidural), while evidence of systemic toxicity was chiefly seen as drowsiness in five patients (1.25 per cent). The only disturbing phenomenon was the high occurrence of irritation on intradermal injection, but this is very likely to be due to the phenol preservative contained in the solution.

The onset of anaesthesia with the agent is fast (4–5 minutes), and this is most in evidence in direct nerve blocks, for example, of the brachial plexus. However, with epidural blocks adequate conditions for surgery may not be present until fifteen minutes after injection. The duration is approximately two hours, with a variation between one and a half and two and a half hours.

Many more blocks than those discussed here have been performed. The group of cases mentioned are typical of the general impression which has been so good that Sympocaine is now our routine agent for nerve blocks.

Summary

In all 413 patients were anaesthetized with Sympocaine 0.5 per cent without epinephrine. Most (175) of the blocks were caudal epidurals with a further 28 sacral and 41 thoraco-lumbar epidural anaesthetics. Possible toxic reactions were observed in 10 patients (2.5 per cent). Hypotension was noted in epidural type anaesthesia and was almost certainly related to the form of block. Temporary irritation occurred on intradermal injection in more than one-third of skin wheals, but this is considered to occur because the experimental solution contains 1:600

phenol. Onset is rapid, usually requiring 4–5 minutes, while duration of action varies between one and a half and two and a half hours. The most common doses for the several techniques are mentioned.

Sympocaine 0.5 per cent used in doses between 15 and 30 cc. has been found to be reliable, to have moderate spreading ability, adequate effect and little evidence of toxic reaction.

Résumé

Nous avons pratiqué, chez 413 malades, une anesthésie avec de la sympocaine 0.5 pour cent sans épinephrine. La plupart des blocages (175) ont consisté en des épidurales caudales et, dans 28 cas, en des sacrées et, dans 41 cas, en des épidurales thoraco-lombaires. Chez dix malades (2.5 pour cent), nous avons observé des réactions qui ont été, il est possible, des réactions toxiques. Au cours des anesthésies épidurales, nous avons observé de l'hypotension qui était sans doute attribuable à la sorte d'anesthésie. Dans 33⅓ pour cent des injections intradermiques, nous avons observé une irritation temporaire, mais à noter que la solution expérimentale contenait 1:600 de phenol. L'induction de l'anesthésie est rapide ne réquérant ordinairement que 4 ou 5 minutes et la durée varie de 1½ à 2½ heures. La Sympocaine 0.5 pour cent employé à des doses variant de 15 à 30 ml. s'est avérée constante d'action, possédant un certain pouvoir de diffusion, assez efficace et laissant de légères traces de réaction toxique.

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ANAESTHESIA FOR TONSILLECTOMY AND ADENOIDECTOMY IN CHILDREN[1]

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THE ANATOMICAL ACCESSIBILITY and doubtful physiological value of the palatine tonsils are responsible for the fact that tonsillectomy accounted for approximately one-third of all operations carried out in the United States since 1924. (1). Depending on geographical location and social environment, 20 to 90 per cent of the population over the age of ten have already had their tonsils removed (2).

Mortality and morbidity are inevitably associated with surgery and are related to the condition of the patient, the nature and extent of the surgery and the efficiency of preparation, anaesthesia and management. Although tonsillectomy is a minor operation carried out on fit children, complications are apt to occur, and there can be no greater tragedy than the death of a healthy child as the result of a minor and perhaps unnecessary operation. Efficient anaesthesia is the main factor contributing to the safety of the patient and the successful removal of the tonsils. Not infrequently the responsibility for administering anaesthesia for this minor operation is delegated to some junior whose experience is limited to single shot "rag and bottle" anaesthesia, or alternatively, an otherwise competent anaesthetist may be prepared to accept the additional hazards imposed by a technique which does not permit complete control. In Britain, according to the Registrar General's figures (2) approximately 40 deaths per year are attributable to misadventures associated with this procedure.

Deaths caused by anaesthesia are invariably preventable, though extenuating circumstances may exist. The majority are caused by overdosage with a potent agent or hypoxia from deficient respiratory exchange. Respiratory obstruction is liable to occur in operations on the upper respiratory tract, and may be due to blood, packs, laryngeal spasm or simple depression of the tongue by retractors. Asphyxia not only endangers the child's life, but if present to even a minor degree will cause an increase in bleeding.

Postoperative pulmonary complications are usually the result of the inhalation of blood or infected material during or immediately after surgery, and prior to the return of the protective reflexes. Steele and Anderson (3) recovered blood from the bronchi of 125 out of 129 patients who were bronchoscoped immediately after tonsillectomy under general anaesthesia and without endotracheal intubation. Waldapfel (4) demonstrated radiologically that fever following tonsillectomy was usually associated with lung infiltrations of various sizes, and that the temperature returned to normal after resolution of these foci. Broncho-pneumonia, atalectasis and lung abscess are the major complications which have been reported following this operation.

Surgical complications and even operative technique are influenced by the conditions made available by the anaesthesia employed. Failure to provide good

[1]Presented at the Annual Meeting, Canadian Anaesthetists' Society, Saskatoon, Sask., June 25, 1957.

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operating conditions for as long as is required will place the surgeon at a disadvantage, make the control of haemorrhage more difficult and lead to incomplete removal of the tonsils. Hyde (5) found residual tags in 68 per cent of 1,000 unselected cases, and this is a grave reflection on the standards of surgery and anaesthesia, either individually or in combination.

Guillotine enucleation, with or without the use of a snare for the removal of the lingual tag, may be successfully performed by a fast and competent surgeon in the short time made available by single shot anaesthesia. The margin for error is narrow, and excessive bleeding, difficulty in removing a scarred and fibrous tonsil or less expert surgery may necessitate longer anaesthesia for the successful completion of the operation. A screaming, coughing, struggling child whose airway may be obstructed by blood has never been an inspiring sight, and thus an effort was made to provide longer and more controllable anaesthesia by oro- or naso-pharyngeal insufflation techniques, posture and suction being employed to keep the airway clear of blood. The increased operating time provided by such methods permitted complete removal of the tonsils by dissection or any other method, but difficulties in maintaining the airway, ventilation and stable anaesthesia were still encountered. Since children are particularly susceptible to the untoward effects of hypoxia and haemorrhage, more adequate control is undoubtedly desirable.

A well-conducted anaesthetic should provide the patient with safety, comfort and minimal sequelae, the surgeon with the optimum operating conditions for as long as he requires, and the anaesthetist with the peace of mind associated with complete control of the situation. The agent and technique selected should therefore aim to provide a pleasant, smooth and rapid induction, stable maintenance, readily controllable depth of anaesthesia, minimal pharmacological upset, adequate oxygenation, and quick recovery of reflexes and consciousness. The airway and respiratory exchange should be under complete control, and aspiration of blood and infected material prevented. The jaw and throat should be relaxed and the optimum surgical exposure and conditions made available without the risk of respiratory obstruction or any other complication.

Endotracheal anaesthesia is therefore essential, and this has already been advocated in 1951 by Slater and Stephen (6) and again in 1953 by Pender and Hallberg (7). Those opposed to intubation claim that it prolongs induction time, requires deeper anaesthesia, may be difficult and traumatic, can lead to reflex vagal inhibition of the heart and that once the tube is in place not only does it get in the way of the surgeon, but may easily become displaced or blocked.

The technique successfully employed in a large personal series of cases, and about to be described in detail, will permit induction and intubation within sixty seconds, complete control of anaesthesia for as long as may be required, and recovery of consciousness within one to two minutes of the conclusion of the operation. Surgical exposure is improved and apart from one freak accident involving the cutting of an endotracheal tube by a guillotine, no other difficulties were experienced.

Repeated electro-cardiograms have failed to reveal any significant abnormalities during intubation or extubation, and this was no doubt due to the prevention of hypoxia, hypercarbia and undesirable "bucking" on the tube. Reflex vagal

inhibition of the heart as a result of irritation of the larynx under light anaesthesia should not, and probably does not, occur provided full oxygen saturation is maintained. Laryngeal stimulation by instruments, suction and packs during the surgical procedure is as great if not greater than that caused by an endotracheal tube, and if intubation is not employed this stimulus may be applied at less desirable levels of anaesthesia and oxygenation. It is therefore apparent that there can be no legitimate objection to endotracheal anaesthesia for tonsillectomy.

Preparation and Premedication

The children are admitted to hospital the day prior to surgery in order that the necessary preoperative assessment and preparation may be carried out. Frank infection is excluded or treated with antibiotics, the haemoglobin, bleeding and clotting times being estimated in selected patients. However, the amount of bleeding which may occur during or after surgery is more frequently influenced by the pathological state of the tonsils, the vascular supply, the mode of enucleation, and the development of postoperative clot.

TABLE I

Pre-Anaesthetic Medication for Infants and Children

Age	Pantopon[a]		Hyoscine[a]
Up to 6 months	nil		Gr. 1/900
6 mo. – 1 yr.	Gr. 1/36	plus	Gr. 1/900
1– 2 yr.	Gr. 1/30	plus	Gr. 1/600
2– 4 yr.	Gr. 1/24	plus	Gr. 1/600
4– 8 yr.	Gr. 1/15	plus	Gr. 1/450
8–12 yr.	Gr. 1/12	plus	Gr. 1/450
12–16 yr.	Gr. 1/9	plus	Gr. 1/300

[a]To be given hypodermically 45–60 minutes preoperatively.

Premedication by the subcutaneous injection of Pantopon and hyoscine in minimal dosages according to age (8) has been found sufficient to obtain the desired effect of mild sedation, amnesia, drying of secretions and reduction of reflex irritability, and without the disadvantage of undue depression. Although hyoscine may be preferred for its amnesic cortical depressant, anti-emetic and more potent anti-secretory effects, one of the authors (M. W. B.) has obtained satisfactory results with atropine in the same dosage.

Heavy premedication and even basal narcosis have been advocated as a means of preventing the psychic trauma occasioned by the barbaric form of anaesthesia so frequently employed. In view of the short duration of the operation and the need for early return of the protective reflexes, the unreliable but prolonged effect of heavy sedation is undesirable and may be dangerous. For this reason the oral or rectal administration of the medium, short or ultra-short acting barbiturates has little place in the management of the routine case. It is, however, possible that extremely nervous or hysterical children might benefit from heavy sedation, but as yet no such cases have been encountered in this series.

In recent years, and without the benefit of premedication, children have been subjected to an increasing number of needles for inoculation, antibiotic therapy,

laboratory investigation, etc., and as yet no adverse psychological effects, such as neurosis or night terrors have been reported. It therefore appears reasonable to assume that efficient venepuncture for the purpose of inducing anaesthesia with Thiopentone would be as effective in removing the fear of anaesthesia from children as it has been for adults. Parents whose children have been exposed to both inhalation and intravenous methods of induction have, by their special requests for the latter method, lent support to this assumption and many have volunteered the information that nightmares did not follow this method of anaesthesia.

Induction

Efficient venepuncture is essential to the success of this technique, and new "23" needles and glass nozzled syringes are used. Since most surgeons work from the right, the left arm is secured to an arm board, before or after induction. Veins of the anterior surface of the wrist or back of the hand are preferred in infants and small children since sudden movement is more easily controlled. Wherever possible the medial aspect of the antecubital fossa is avoided. In most patients little difficulty has been experienced in finding a suitable vein, though on occasion a vein in the dorsum of the foot has had to be used. Selection of the site of injection, palpation of the vessel before or after application of the venous tourniquet (that is, at a pressure insufficient to occlude the radial pulse) combined with careful observation should preclude the possibility of inadvertent injection of Thiopentone in or near an artery.

In spite of the light premedication, few children raise any objection, and this is in part due to the friendly distraction provided by the nurses. Occasionally a small child may be reluctant to lie on the table, and if this is the case he is induced in a sitting position, or more rarely still, in the arms of a nurse whose maternal instinct will not allow her to surrender a forlorn infant. A tearful induction is therefore the exception rather than the rule.

The routine induction dose of Thiopentone is 25 mg. (1 ml. of 2½ per cent) per 10 lb. of body weight, and this may be increased or decreased 25 per cent depending on the speed of the surgeon, the age and build of the child, and the effect of the premedication. For an average operating time of 5 to 15 minutes the routine dose has proved satisfactory and is administered as quickly as possible. The Thiopentone syringe is then changed for one containing 2–5 ml. of succinylcholine (depending on the size of the child, and the anticipated duration of the operation) and the appropriate dose of 5 mg. (⅛ ml. Scoline) per 10 lb. of body weight is rapidly injected. Since the intermittent injection of succinylcholine is an integral part of the technique, the syringe is strapped in place with adhesive tape, a small strip of which is used to hold the plunger and prevent aspiration of blood which might block the needle.

The unconscious and apnoeic child is hyperventilated with oxygen for 15 to 20 seconds prior to oral insertion of a suitable endotracheal tube under direct vision. Upper respiratory obstruction interfering with oxygen inflation may be relieved by insertion of an oro-pharyngeal airway, but in spite of the fact that many of the smaller children had tonsils meeting in the mid-line, this airway

was seldom required. Continuous oximeter readings indicated that this hyperventilation with oxygen maintained the oxygen saturation in excess of 95 per cent for two or more minutes of complete apnoea. The complete relaxation and the adequate time available contributed to the ease with which atraumatic intubation could be carried out, and thus provided excellent conditions for the residents to gain practical experience in intubation.

Intubation

The basic equipment, as illustrated in Figure 1, is prepared prior to induction.

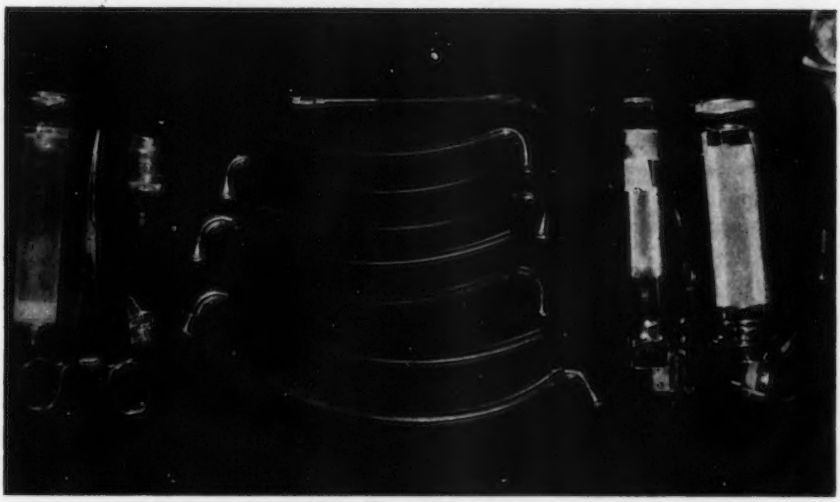

Figure 1. Basic equipment for intubation of children.

A selection of McIntosh blades may be an advantage, but the medium adult blade has been found to give good exposure in almost all children over 30 pounds in weight, the No. 1 Miller blade being preferred for smaller children and infants.

The endotracheal tubes used may be rubber, portex or of other plastic material, and a complete selection of sizes must be available. Irrespective of composition these tubes should maintain their curve for ease of insertion, be firm enough to prevent obstruction by minor degrees of external pressure or kinking, and yet not too firm or the desired leak-proof fit for inflationary pressure of 10–15 mm. of mercury might not be obtained without undue pressure thus predisposing to postoperative irritation and oedema of the cricoid region in infants or the larynx in children.

The selection of the correct size of tube is important, since attempts to pass too large a tube will produce local damage leading to postoperative coughing, hoarseness and stridor, whereas too small a tube will permit aspiration of blood. If the tube used allows an appreciable leak of anaesthetic gases at inflationary pressures of less than 10 mm. mercury, it should be changed for the next larger

size. Although maintenance of a positive pressure of 3–4 mm. of mercury during both inspiratory and expiratory phases of the respiratory cycle will prevent the aspiration of blood–this has been confirmed by postoperative endotracheal suction via the endotracheal tube–there is troublesome "bubbling" in the presence of even a little blood in the throat, and the raised intrapulmonary pressure will raise venous pressure and may therefore increase bleeding.

The selection of the tube to be used is based on age, weight and build of the child, and confirmed by examination of the larynx prior to intubation. A good exposure of the larynx is required, and if there is any resistance to the insertion of the tube a smaller one is used. With increasing experience, the initial choice should almost invariably be correct and the trial and error method should not be necessary. The sizes of the oral rubber Magill tubes used in 1,000 consecutive cases have been classified according to the ages and weights of the children, (Table II). It should be noted that the rubber and Portex Magill tubes have a different system of numbering–for example, the rubber size 0 is larger than the Portex size 1.

TABLE II

Weight (lb.)	Tube size	Age in years										
		Under 1	1	2	3	4	5	6	7	8	9	10–15
Under 20	0	4	5									
			2									
21–25	0		4	3								
	1		11	13	1							
26–30	1	1	10	19	13	2						
	2		3	19	21	4	1					
	1			8	7	4						
31–35	2		1	33	69	26	9					
	3			1	4	7	2					
	2			6	26	29	14	4	1			
36–40	3			1	6	23	38	10	1			
	4				1	4	5	3	2			
41–45	3				4	14	39	22	2			
	4					3	15	14	6	1		
	5				1	3	3	12	4	2	1	
46–50	4					5	5	20	11	3	1	
	5						2	9	10	3	1	
	4				2	2	4	13	9	2		1
51–55	5						3	10	16	8	3	1
	4–c							4	2	2		1
	4						2	3	6	7	3	
56–60	5						2	1	9	3	4	3
	4–c							3	9	9	3	2
	4						1	1	1		1	2
60–70	5								4	2	5	1
	4–c							2	4	7	11	7
Over 75	4 & 5 & 6–c							1		3	6	95

The tube should preferably extend to the middle third of the trachea, and in this series a standard length for each size of tube has proved satisfactory. Too short a tube may be dislodged during the operation and too long a tube will reach the more sensitive lower trachea and carinal region and predispose to coughing prior to the removal of the tube, at the conclusion of the operation. With

the tip of the tube held at the entrance to the larynx an estimate of the optimum distance for insertion can be made in relation to the length of the tube remaining outside the mouth.

The acutely curved Magill nasal endotracheal adapters more closely approximate to the sharper angle created by the mouth gag, thus permitting the endotracheal connector to lie in closer apposition to the face and reducing the danger of kinking the smaller endotracheal tubes.

The tubes, which have been washed with soap and water but not sterilized, are lubricated with a sterile non-anaesthetic, water-soluble jelly since the increased risk of postoperative aspiration outweighs any advantages associated with the use of an anaesthetic lubricant. During insertion contact with any infected material from the nose and throat is avoided, and in this series there were no postoperative respiratory complications.

Following induction and intubation the mouth gag is inserted and the tube with Magill adapter attached is led through the gag prior to attachment to the rubber end of the endotracheal connector of a partial rebreathing or circle circuit. The tube is then fixed on the side of the mouth apposite to that from which the first tonsil is to be removed. This whole procedure can be carried out in less than forty seconds, but sixty to ninety seconds is the more usual unhurried induction time.

Maintenance and Management

Maintenance is with a nitrous oxide–oxygen (25–50 per cent) mixture, adequate ventilation being assured by controlled or assisted respiration via any type of anaesthetic circuit. Complete control of palatal reflexes, respiration and movement is obtained by the intermittent administration of succinylcholine in dosage of 25–50 per cent of that used for induction—the amount given depending on the length of the original apnoea and the anticipated duration of the operation.

Hyperventilation in a circle circuit with absorption will lower the blood carbon dioxide thus prolonging apnoea of the relaxant and potentiating anaesthesia by the analgesic effect of the reduced cerebral circulation, but the increased resistance of the circuit may, in smaller children, increase venous bleeding, though to a lesser extent than with even minor degrees of asphyxia. The nitrous oxide–oxygen mixture may be supplemented with 10 per cent cyclopropane if desired, but this is by no means necessary unless perhaps on the very rare occasions when the succinylcholine syringe becomes dislodged and cannot easily be replaced. A low resistance partial rebreathing circuit permits the addition of Trilene, analgesic concentrations of which will permit spontaneous respiration without breath-holding or coughing, and provide a short period of postoperative analgesia, thus reducing restlessness. Fluothane has also been used, but no particular advantages related to reduction in bleeding or tolerance of movement of the endotracheal tube under light anaesthesia have been observed.

Management during operation depends to some extent on the individual surgical technique. After guillotine enucleation the anaesthetist may, by external pressure on the neck, assist the surgeon in grasping the lingual tag for removal by a snare. When the first tonsil has been removed, either by guillotine or dissection, and the surgeon is ready to attack the remaining tonsil, the pressure on

the tongue depressor should be released to permit the tube to be moved to the other side of the mouth. If spontaneous respiration has returned, it is advisable to administer a further small dose of succinylcholine lest coughing be associated with movement of the tube.

Even in an infant the presence of an oro-endotracheal tube does not inconvenience the surgeon by encroaching on the operative field; on the contrary, the surgical exposure is improved because the tongue can be freely retracted without fear of obstructing the airway. Early in this series approximately 400 consecutive patients were intubated by the nasal route under direct vision, Magill's angled forceps being used to direct the tube through the larynx, thus avoiding trauma to the cords or cricoid region. The advantages related to secure fixation, absence of movement of the tube and doubtful improvement of surgical exposure were outweighed by the disadvantages of having to remove the tube prior to the return of consciousness so that the adenoidectomy could be carried out. Adenoidal obstruction to the passage of the tube could be overcome, but the danger of introducing infected material to the trachea existed, even though the end of the tube was cleaned by swab or suction prior to insertion into the larynx.

When both tonsils have been removed and bleeding controlled, the table is placed in a five to ten degree Trendelenburg position and adenoidectomy carried out. If the dosage of succinylcholine has been properly estimated, spontaneous respiration should be returning and when 100 per cent oxygen is administered the child will recover consciousness within one to two minutes. During this time adenoidal bleeding is arrested and a final examination and aspiration of the throat carried out. The succinylcholine syringe is removed and pressure applied to prevent formation of a haematoma. Provided the tube is not moved, most children will recover consciousness without coughing and extubation is then carried out either before or immediately after turning to the semi-prone position. It is preferable to remove the tube at the peak of inspiration so that an expiration cough or cry will be the first reaction.

Coughing or laryngeal spasm may be associated with pre-existing respiratory infection, irritation of the larynx or trachea by trauma or blood, the existence of hypoxia, or by extubation at a certain stage of lightening anaesthesia. Oxygen saturation prior to removal of the tube will prevent hypoxic perpetuation of minor degrees of breath-holding or spasm, and proper management should prevent this complication. Should spasm occur, the response to Trendelenburg, suction and oxygen inflation by mask is usually immediate, though re-intubation was carried out in two cases where there was bleeding.

Recovery

The conscious or semi-conscious child is removed from the operating room in the semi-prone position with a pillow under the chest. Such patients are kept in a well-equipped recovery room for 15–20 minutes to ensure that there is no further bleeding, and if left undisturbed most children will rest quietly. Swallowing of blood is discouraged since not only does this predispose to postoperative nausea and vomiting, but may hide continued bleeding. Repeated recordings of the pulse and examination of the throat will reduce this hazard.

Review of Cases

During the last four years this technique has been used on 3,262 patients between the ages of 1 and 15 years, the number being distributed as follows:

Age in years	*0–1*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10–15*
No. of cases	15	123	350	467	447	462	430	287	190	121	370

Difficulties and complications have been remarkably few in number.

Induction

Comparative peace and quiet has replaced the anguished screams which used to emanate from the ENT theatres on tonsil mornings. Only two children were subjected to unsuccessful attempts at venepuncture, and in four, venepuncture was not attempted because the veins were poor (2 cases) or because the inhalation method was requested (2 cases). In the latter two cases, the children were induced with a nitrous oxide–cyclopropane or nitrous oxide–trichlorethylene mixture, after which succinylcholine was given to speed up intubation and permit control of palatal reflexes under a lighter plane of anaesthesia. With increasing experience induction difficulties are rarely experienced, though on occasion a vein in the dorsum of the foot was the only one to be found.

Intubation

Unhurried atraumatic intubation was made easy by the conditions provided. Obstruction to the tube by kinking or compression by tongue depresser or guillotine is easily diagnosed by the "feel of the bag" and just as easily remedied —though it may be permitted to exist for thirty seconds or so for the convenience of the surgeon. Right endobronchial intubation did not occur, but could easily be remedied by slight withdrawal of the tube. Accidental displacement of the tube occurred in one case during adenoidectomy but did not require replacement. On one occasion a tube was cut by a guillotine, and the distal portion, which slipped into the trachea, required immediate bronchoscopic removal; subsequent progress was uneventful. As mentioned above, minor degrees of laryngeal spasm occurred infrequently and were due chiefly to impatient removal of the tube. In two cases re-intubation was required by the development of cyanosis in association with a recurrence of bleeding, which made inflation by mask unwise. No postoperative respiratory complications associated with intubation or aspiration were observed.

Anaesthesia

Delayed recovery of spontaneous respiration is usually due to too recent or too large a dose of Scoline, and artificial ventilation for a few minutes postoperatively is all that is required. However, a genuine sensitivity to the induction dose did occur in one 3-year-old girl, and 1½ hours artificial ventilation with oxygen preceded recovery. Her little brother, aged 2, was apnoeic for 20 minutes following ⅛ the normal dose of succinylcholine. Both children had a low pseudocholinesterase level as a result of the fumigation of a basement with an anticholinesterase insecticide. One morning four consecutive patients, although breathing well, failed to wake up within a few minutes of the conclusion of the

operation. Investigation showed that inadvertent overdosage of Pentothal had taken place as a result of failure to mix one of the bulk solutions properly. Uneventful recovery of all four patients within periods of ½–1½ hours took place. No other anaesthetic difficulties were encountered during or after operation.

Surgical Complications

Bleeding during operation was not increased, and the ideal conditions provided for the arrest of haemorrhage reduced the incidence of immediate postoperative bleeding. The unlimited time available permitted careful removal of tonsils by expert and tyro alike.

Summary and Conclusions

The children undergoing, and the surgeons performing, tonsillectomy have for too long been denied the safety, comfort and operating conditions made possible by modern anaesthesia. Although this is a minor operation complications are apt to occur, and the cause and prevention of these are discussed. A technique which has proved safe, efficient and free from complications in a personal series of 3,262 cases over the last four years will permit induction and intubation within 60–90 seconds, complete control of anaesthesia for as long as may be required, and recovery of consciousness within 1–2 minutes of the end of the operation.

This technique is based on light premedication, intravenous induction with Thiopentone (25 mg. per 10 lb. of body weight) and succinylcholine (5 mg. per 10 lb. of body weight) and hyperventilation with oxygen prior to oral intubation. Maintenance is by artificial ventilation with nitrous oxide–oxygen, with or without minimal trichlorethylene, the intermittent administration of succinylcholine (¼–½ induction dose) being used to potentiate anaesthesia, control respiration and provide a quiet, relaxed throat. The endotracheal tube is kept at the side opposite to that on which the surgeon is working, and extubation is carried out in a Trendelenburg or semi-prone position on recovery of consciousness at the conclusion of the operation.

The surgeons appreciate the more rapid induction, better operating conditions and reduction in operative and postoperative complications, and it is felt that the advantages of endotracheal intubation are so apparent that reluctance to intubate can only be caused by inadequate equipment or poor technique. This selection of agents and technique, with or without minor variations, has been found of value in a variety of operations on infants and children.

Résumé

Il y a déjà trop longtemps qu'on prive de la sécurité, du confort et des conditions opératoires rendues possibles par l'anesthésie moderne et les enfants qui subissent l'amygdalectomie et les chirurgiens qui pratiquent cette opération. En dépit du fait que cette opération est mineure, il est susceptible de survenir des complications, puis nous en discutons les causes et la prévention. Au cours des

quatre dernières années, dans une série de 3,262 cas, nous avons employé une technique qui s'est avérée de toute sécurité, efficace et exempte de toute complication: elle nous permet de faire l'induction et de pratiquer l'intubation en deçà de 60 à 90 secondes, d'avoir un contrôle complet de l'anesthésie aussi longtemps qu'on l'exige et d'avoir un retour à la conscience en deçà de 1 à 2 minutes après la fin de l'opération.

Cette technique consiste en une prémédication légère, une induction au Thiopentone par voie intraveineuse (25 mg. par 10 livres de poids) et de la succinylcholine (5 mg. par 10 livres de poids), puis une hyperventilation avec de l'oxygène avant l'intubation orale. On maintient l'anesthésie par da la respiration artificielle avec du protoxide-oxygène avec ou sans des traces de trilène, puis on répète des doses intermittentes de succinylcholine (¼ à ½ la dose de l'induction) pour potentialiser l'anesthésie, contrôler la respiration et procurer une gorge calme et relâchée. Nous plaçons le tube endotrachéal du côté opposé à celui où le chirurgien travaille et nous pratiquons l'extubation en position de Trendelenbourg ou en position semi-ventrale au retour de la conscience à la fin de l'opération.

Les chirurgiens apprécient l'induction rapide, des conditions opératoires améliorées et la diminution des complications per et post-opératoires et il semble que les avantages de l'intubation endotrachéale sont tellement transcendants que seulement une instrumentation inadéquate ou une mauvaise technique pourraient justifier de ne pas intuber. Ce choix des agents et de la technique, avec ou sans modifications mineures, s'est avéré précieux dans une variété d'opérations chez les bébés et les enfants.

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PNEUMOPERITONEUM–A COMPLICATION OF NASAL OXYGEN THERAPY: A CASE REPORT

E. A. GAIN, M.D.[1]

PNEUMOPERITONEUM IS usually the result of a perforation of the stomach or bowel by disease or mechanical trauma. This type rarely results in tension causing respiratory and circulatory embarrassment. Pneumoperitoneum can follow mediastinal emphysema produced by excessive airway pressure during anaesthesia (1, 2); the gas tracking down retroperitoneal and breaking through the peritoneum, but this is very rare (2). Everyone is familiar with the rather frequent error of attaching the oxygen to the gastric suction tube, an accident which is easily recognized.

We believe that the following case is of interest because of its rarity and its similarity to a case reported by Fenton (3) of pneumoperitoneum following nasal oxygen therapy.

Mrs. S., a healthy 53-year-old female, was prepared for biopsy of a tumour of the right breast and possible radical mastectomy. Anaesthesia was induced with 0.25 gm. Thiopentone followed by 25 mg. Meperidine and nitrous oxide–oxygen 4:2 administered by a semi-closed circle absorption system. The respirations were assisted throughout but not controlled. There was a fifteen-minute delay between induction and the commencement of surgery. With the skin incision mild laryngospasm developed and was easily corrected in a very short time with Thiopentone 0.125 gm. Meperidine 25 mg. increased assistance to respiration. The anaesthetist did not consider that excessive pressure was used at this time and it was definitely less than 20 mm. Hg.

At the conclusion of the 20 minutes of surgery respiration was only 6 per minute so Nalline® 5 mg. was given intravenously. The rate increased to 12 per minute and the patient was returned to the recovery room in good condition. Nasal oxygen by catheter was ordered in case respiratory depression should recur. The patient arrived in the recovery room and nasal oxygen at 8 litres per minute was commenced at 11:40 A.M. At 12:20 P.M. the recovery room nurse reported that the patient was in shock and not responding as rapidly as was expected; anaesthesia seemed deeper if anything. Examination revealed a deeper state of anaesthesia than one would expect, rapid predominantly thoracic respiration, systolic blood pressure of 70 and pulse of 74. The skin was pale, dry and cold; the abdomen was grossly distended, tympanitic, rigid, and palpation caused some pain-like response. At first only gastric distension was suspected, but because of tenderness X-rays were taken of chest and abdomen. In the meantime attempts to pass a gastric tube failed because of an apparent obstruction at the level of the cardia. The X-rays revealed a normal chest except for high diaphragms, a massive pneumoperitoneum and a distended stomach but no excess of gas in the small bowel. Displacement of the stomach was most probably the reason the gastric tube could not be passed.

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A needle was inserted through the abdominal wall and gas under marked pressure gushed forth, the abdomen collapsed and was then soft with no evidence of peritoneal irritation. The patient's conscious level improved rapidly, undoubtedly because of the improved ventilation, and the blood pressure soon returned to normal levels.

Postoperatively the patient had an elevated temperature (99°–101°) for two days and shoulder pain, the abdomen remained soft and not tender, no other evidence of peritonitis occurred and the patient was discharged well after five days of observation.

Two days later the patient was readmitted with the typical signs and symptoms of a left lower lobe pneumonia. Under conventional therapy this resolved rapidly and the patient was discharged and has remained well. During the last admission complete radiographic examination of chest, oesophagus and stomach were carried out, no abnormalities other than the resolving pneumonia were discovered.

At the time of the pneumoperitoneum it was believed that in spite of the anaesthetist's assurance that no excessive pressure had been used in assisting respiration this was the most likely cause of such a massive pneumoperitoneum. Fenton's (3) report of a similar case following nasal oxygen therapy was recalled and it is believed that the same sequence of events occurred as described by Fenton (3). She postulated that the nasal oxygen catheter had been inserted below the cricopharyngeus which acted as a true sphincter, and with a relaxed cardia and closed pylorus allowed distension and perforation of the stomach.

At autopsy Fenton's patient showed that the muscle fibres of the stomach were laminated and separated and there was a minute tear in the mucosa and extensive bleeding into the stomach and intestine. Since she does not mention the mode of exit of the oxygen from the stomach into the peritoneal cavity, one must assume a tear on the peritoneal surface of the stomach or intestine. As there was no sign of peritoneal irritation in our patient, it is suggested that possibly the gas had passed beneath the mucosa and out along the vessels of the stomach into the peritoneal cavity, as it does, in a similar manner, in mediastinal emphysema following alveolar rupture due to excessive airway pressure during anaesthesia (1, 2).

We cannot feel as absolutely certain of the aetiology in this case as could Fenton (3), an endotracheal tube was not used here and we believe that one could have overlooked the distension because of the surgical drapes and the site of the operation, and the cause therefore could have been excessive mask pressure. On the other hand, we doubt if the patient would have been considered to be in good condition if this distension had been present in the operating theatre or on arrival in the recovery room, and therefore the most likely cause was the nasal oxygen.

Measurement of the oxygen flowmeter used revealed that a pressure of 40 mm. Hg was necessary to open the safety blow-off, this is undoubtedly an excessive pressure and such therapy apparatus should be manufactured to blow-off at a much lower pressure or this complication will continue to occur. Fenton's case resulted from the same fault, in her case a flowmeter was not used, only a simple pin-type valve with no pressure regulation.

This case again emphasizes the dangers of oxygen therapy using a nasal catheter, also the need for care in placing the catheter correctly and the use of low-pressure controlled flowmeters.

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PREOPERATIVE EXAMINATION AND PREPARATION OF PROBLEM PATIENTS[1]

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TODAY'S WIDENING SCOPE of surgery, allowing help to even the poorest of "risks" depends on team-work. The problems are discussed by all who can bring their special knowledge into play. The anaesthetist should not and cannot be missing from this team and must be as conversant in present-day medical knowledge as the best on the team.

Interference with the proper function of the cardio-respiratory system and circulatory system due to disease or injury constitutes the most commonly encountered problems in anaesthetic practice. Closely related are problems arising from disturbed fluid and electrolyte balance and from altered body resistance to stress.

This division, of course, is an artificial one, as actually they may all be present at the same time or merge from one into another if unattended; furthermore, this grouping does not include all the diverse problems which crop up in anaesthetic practice.

An endeavour is made to cover the most frequently encountered problems, to illustrate them by pertinent cases and to group them only for the sake of clarity.

RESPIRATORY SYSTEM

The gas exchange in the lungs is commonly impaired by a combination of inadequate aeration or perfusion. Interference with the bellows action of the lungs and respiratory muscles may result from the depression of the driving mechanism (respiratory centre), inflammatory, neoplastic and degenerative disease of lungs and bronchi; changes in the thoracic cage caused by disease, degeneration or trauma. The results are disturbed relationship between the amounts of air present in the lungs and the amount of fresh air entering the alveoli at rest and during the exercise; reduction of respiratory reserve available to an individual at the moment of stress; changed pressure relationship between the intra-pleural space and the atmosphere.

Well-ventilated alveoli may fail as respiratory units if pulmonary circulation is inadequate. The latter may be the result of the reduced number of patent capillaries, sluggish circulation due to a failing heart (usually associated with pulmonary hypertension), and the reduced amount of circulating blood volume and haemoglobin due to haemorrhage and shock.

The respiratory system is usually examined together with the cardiovascular system, and a statement "heart and lungs . . . normal or negative" is made. When abnormal, a listing of abnormal signs and symptoms usually follows. The importance of the pre-anaesthetic visit lies in the evaluation of the patient as a risk.

[1]Read at the Nova Scotia Division of Canadian Anaesthetists' Society Annual Meeting held on April 15, 1957, at Victoria General Hospital, Halifax, N.S.

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In other words, one endeavours to estimate patient's reserve to withstand drugging of the respiratory centre, interference with respiratory excursions of the diaphragm and the thorax by abnormal positions and use of relaxants, periods of relative or complete respiratory obstruction, haemorrhage, etc.

Many tests have been devised to measure practically all phases of ventilation and perfusion, but most of them are time-consuming and require equipment not ordinarily available.

Two simple tests allowing measurement of ventilating capacity of an individual, requiring minimum preparation and only standard spirometric equipment are available (1). They are the "Timed Vital Capacity Test," and the "Maximal Breathing Capacity Test." Vital capacity, although useful in measuring changes in the same individual over a period of time, being solely a volume measurement does not take time and effort into consideration. Thus an emphysematous patient may have a fairly large vital capacity but require increased time and effort to expel it. The 3-second Timed Vital Capacity Test gives the maximal volume of the vital capacity that can be used by the individual (2).

Normal values	*1st. sec.*	*1st two sec.*	*1st three sec.*
% V.C.	83%	94%	97%

In the "Maximal Breathing Capacity Test," the volume of air that can be breathed as the maximal effort, in one minute, is measured. This gives information on ventilating efficiency of the respiratory muscles against normal and abnormal forces, resistant to the movement of the air in and out of the lungs.

The "Formula of Motley" allows prediction of the values of "Maximal Breathing Capacity" for a given sex, age and body surface area:

$$\left(F^{3} - \frac{\text{Age}}{2}\right) \times \text{BSA (Body Surface Area in sq. metres)}.$$

The simple, standard exercise "step test," performed at the bedside will give a rough measure of disability in a patient suspected of suffering from cardiopulmonary insufficiency. The subject steps up and down on a 20 cm. stool 30 times in one minute. Moderate pulmonary or cardiac disease leads to dyspnoea for at least two minutes. Severely handicapped patients remain dyspnoeic for several minutes. Normal individuals show no significant dyspnoea.

Knowing the individual's maximal breathing capacity and the amount of air breathed at rest over the same period of time (resting minute volume), an idea can be formed of that individual's breathing reserve:

$$\frac{\text{Maximal breathing capacity} - \text{Resting minute volume}}{\text{Maximal breathing capacity}} \times 100 = \text{Breathing reserve percentage.}$$

At rest, this amounts to 95–91 per cent of maximal breathing capacity, up to the fifth decade of life. During the first minute of rest following standard exercise, the breathing reserve is reduced to 88–70 per cent in younger patients and 75–45 per cent in the older age group. These values, obtained in healthy individuals, may be appreciably changed in those suffering from cardio-respiratory

[3]Females: F = 83; males: F = 97.

disease. The extent of reduction of the breathing reserve is of utmost importance to those who may plan to interfere in one way or another with diseased respiratory systems.

The choice of anaesthetic and conduct of anaesthesia will be based on the information gained from the history, physical examination and those few tests. No chance should be missed to improve the existing respiratory disability even though the eradication of the factors responsible for the dysfunction is impossible.

Treatment of congestive heart failure with digitalis, salt restriction and diuretics goes a long way towards improving pulmonary circulation, allowing for faster circulation of the blood in the alveoli, diminished pulmonary hypertension and a dryer lung. Expansion of the lung can be improved by draining the co-existing pleural effusions or ascites. The haemoglobin and blood volume should be brought as close to normal as possible, with blood transfusions, using whole blood or packed cells. Concomitant hypoxia has to receive attention with oxygen inhalation through a mask or through a nasal catheter (12–18 F.) with flows not less than 6–8 litres per minute.

Bronchial obstruction from secretions will have to be treated. Antibiotics alone or in combination with aerosol sprays, containing vasoconstrictor drugs, do not always suffice. Postural drainage, catheter aspiration of the trachea through a bronchoscope, and restriction of cough-depressing drugs are often necessary. One reads more and more of the advisability of performing early elective tracheotomy in cases where clearing of the tracheobronchial tree gets out of hand with conservative measures. At this juncture, the anaesthetist's stand may well tip the scale of pros and cons. Considering that tracheotomy in no way interferes with subsequent conduct of anaesthesia, and that it rather facilitates the handling of the patient, one might think that he will favour the tracheotomy.

The value of preparation of asthmatic patients with cortisone is well established, and the value of Largactil as a premedication sedative without fear of respiratory depression has been stated.

Case 1

Mr. R. P. G. (age, 56; weight, 160 lb.) suffered a fractured hip. He was admitted late at night. On admission it was noted that he had a marked breathing difficulty from asthma. His respiration was laboured, and expiratory wheezing and much grunting were present. He was slightly cyanosed about his lips. Patient's relatives stated that he spent most of his time in bed, unable to lie down on account of his asthma, which started four years previously, soon after a lobectomy operation for bronchiestasis. The patient had been conveyed to the hospital sitting in an armchair; the latter having been placed on top of a truck.

On examination, the patient's respiratory rate was 20/min., his pulse was 120/min., and his blood pressure 150/90. His breathing was mainly diaphragmatic and his abdomen protruding. On auscultation generalized rhonchi were heard but few rales were present. The breath sounds were fairly loud except on the lobectomy side, where they were either diminished or absent. The heart was not enlarged and there were no murmurs. There also were no signs of congestive heart failure. Marked finger-clubbing was noticeable. X-ray of the chest revealed no additional findings. EKG was essentially normal except for left ventricular preponderance. Laboratory data have shown slight leukocytosis to be present.

The patient was placed in Fowler's position, and he would not allow any other position, and oxygen was started at 7 litres/min. through a nasal catheter. He then was given Demerol 50 mg. and Largactil 25 mg. intramuscularly and Meticorten 2.5 mg. These allowed him to spend a fairly comfortable night. In the morning, the medication was repeated and when it took its effect, the head of the bed was gradually dropped to about 20° from the horizontal. There was no change in the pulse or respiratory rate.

Premedication consisting of Largactil 25 mg. and Demerol 50 mg. was given intramuscularly in the afternoon and the patient's fractured hip was pinned under spinal anaesthesia, using oxygen 7 litres/min. and Neosynephrine intravenous drip (1 mg. per 100 cc.) as supportives. The patient tolerated the supine position and the operation very well.

It is common knowledge that heavy cigarette smoking is associated with increased secretions and apparent over-activity of the mucosa of the upper respiratory passages. These tendencies seem to increase following general anaesthesia leading to discomfort and posing the danger of atelectasis. There is little one can do, in the last day or two before the operation, in order to alleviate this threat. An opinion has been expressed that smoking should be forbidden or curtailed to a minimum, for at least two weeks before the proposed operation. This rule is most important in those facing abdominal or hernia operations.

Certain conditions resulting from chest injuries demand immediate treatment to correct altered respiratory mechanics incompatible with life (3). In the open pneumothorax, when injury has caused a rent in the thoracic wall larger than the glottic opening, a complete or near-complete collapse of the lung occurs and a "mediastinal swing," sufficient to interfere with expansion of the contralateral lung, takes place with each inspiration. This "swing" also interferes with the venous return and the filling of the right heart, leading to a progressive fall in cardiac output, and aggravating shock. It is imperative to re-establish negative pressure in the affected side in order to permit re-expansion of the lung and to abolish the "swing" of the mediastinal structures. The institution of positive-pressure oxygen breathing and temporary dress-sealing of the wound are the first steps before any surgical action.

In a crushed chest, or "stove-in" chest, the rigidity of the chest wall is destroyed. "Paradoxical respiration" may be present in this type of injury, when the involved area becomes indrawn on inspiration and protrudes on expiration. This may cause little or no air movement in and out of the chest, depending on the extent of the injury. Here again, immediate treatment is necessary to preserve life; assisted respiration with oxygen or air, and fixation of the injured side by strapping and making the patient lie on the affected side are the first-aid measures which the anaesthetist may be called upon to perform.

The presence of varying amounts of blood in the pleural space is a rule rather than an exception when thoracic injury has occurred.

The loss of blood from a rent in the lung may be quite appreciable and, in some cases, out of proportion to the chest wall injury. It has occurred in at least two cases known to the author, in the absence of any penetrating chest wall injury.

Case 2

Mr. R. A. M. (age, 36; weight, 160 lb.) suffered a gun-shot injury to his chest; on admission he was restless and apprehensive but not in shock. His blood pressure was

150/90; pulse rate 90/min.; respiration 24/min., laboured on account of pain and associated with haemoptysis. There was surgical emphysema present extending to the neck and the patient's face was congested, but there was no cyanosis. The movement of the left side of the chest was impaired. Large dressing prevented detailed examination of this side of the chest. X-ray of the chest showed fluid density from the third rib down.

It was decided to establish an under-water drainage of the left pleural cavity and to explore and debride the wound in the chest wall. Quick intubation under general anaesthesia was followed by the toilet of the trachea. The patient was then turned on his side, injured side uppermost. Soon after, the debridement was started and it was then noted that the patient's blood pressure fell to 90 mm. Hg systolic and the pulse and respiration became more rapid. The pleura as yet not having been opened, it was suspected that more than average amount of bleeding occurred into the pleural cavity.

The left side of the chest was then opened through a wide incision and after the retractors were placed the lower lobe of the left lung was found to be collapsed and upwards of 1,000 ml. of blood was evacuated. On inflating the collapsed lung, a rent in the lingular lobe was identified. Following the repair of the torn lung, the chest was closed and drainage of the pleural space instituted. Blood was replaced by transfusion during the procedure.

There was no evidence that the bullet had penetrated the parietal pleura.

When the diagnosis of persistent haemorrhage into the pleural space is made, surgical intervention in order to control the bleeding is the only reasonable method of treatment. Prompt replacement by transfusion of blood lost should be concomitant with early intubation, preferably under topical anaesthesia, which will allow satisfactory toilet of the tracheobronchial tree. Early tracheotomy should be considered if intubation proves difficult or is inadvisable for any reason (4).

Many surgical procedures on patients with less severe chest injuries may be performed satisfactorily under local or block-type anaesthesia.

Treatment of shock, establishment of adequate airway and correction of abnormal respiratory physiology are the most important steps before any further action is taken in thoracic injury.

Heart and Circulation

The number of patients suffering from heart disease, facing elective or emergency surgery, exclusive of surgery on the heart or great vessels, is steadily increasing on account of the longer survival rate of the general population. Although these patients still represent a definite risk, particularly if other disorders are present, the majority of them go through surgery successfully. For instance, the mortality rate among those suffering from coronary insufficiency with a history of one or more episodes of acute coronary infarction, has fallen considerably as shown by the following reports (5).

1929	21.8%	(170 cases)	Sprague
1930	12.1%	(414 cases)	Butler and Feeney
1939	4.3%	(259 cases)	Brummer and Williams
1948	9.9%	(311 cases)	Morrison
1951	5.2%	(58 cases)	Hannigan *et al.*
1955	5.7%	(70 cases)	Baker, Gromer and Wise
	3.6%	(111 procedures)	

Improved anaesthetic management has certainly played a part in this progress. Pre-anaesthetic evaluation, the knowledge of the nature of the dysfunction of the cardiovascular system and appropriate preparation constitute the better part of that management. Evaluation of the reserve based on clinical examination and history, supplemented by special tests, is the one single step of paramount importance.

Inquiry into the performance of daily activities, the occurrence of shortness of breath or pain in the chest on exercise, nocturnal attacks of "asthma," frequent fainting and dizzy spells, a history of prolonged periods of bed-rest during pregnancies on account of a "weak heart" will all throw much light on functional capacity and amount of actual disability.

Careful attention paid during physical examination to the presence of venous congestion, basal crepitations, pre-sacral or ankle oedema, irregular pulse as well as dyspnoea or cyanosis will prove or disprove the presence of congestive heart failure. Of whatever origin, this is the gravest complication, demanding energetic treatment before any kind of surgery, elective or emergency. Detection and treatment of early stages of congestive heart failure will prevent its appearance on the operating table.

In old people, the presence of slow, irregular pulse, particularly if of long standing, is not taken with the same gravity that it is in young persons. However, rapid pulse, regular or irregular, due to fibrillation, frequent extrasystole, or paroxysms of the tachycardia calls for investigation as to the cause and appropriate treatment before anaesthesia.

Marked dyspnoea and tachycardia lasting two or more minutes following a simple standard exercise, as described under respiratory tests, shows the existence of cardiopulmonary inefficiency.

All this information is to be found right at the bedside with no more complicated equipment necessary than a pair of eyes and a stethoscope, and no amount of descriptive work in the chart will take its place. The anaesthetist has to evaluate his patient for himself and must not rely entirely on notes, EKG reports or hearsay statement of optimistic nature.

The tangible evidence thus obtained by physical examination may then be measured against the unknown factors such as the effect of anaesthetic, the length of the operation, the amount of bleeding, the position on the table, etc. In other words, the evaluation of the reserve must precede any discussion of the risk involved in undergoing surgery.

Knowledge of the nature of the heart disease and the amount of disability caused is indispensable in planning the treatment. The latter will be aimed at reducing incapacity to a minimum. Postponement of the operation altogether, on account of the heart disease, will seldom be necessary. In the presence of the actual emergency (perforated ulcer, ruptured gall bladder, intestinal obstruction or obstetrical emergency) one has to take the risk in order to save life.

In cases of recent myocardial infarction, it is suggested that at least six to eight weeks should elapse between the attack and surgery. The use of anticoagulants carries additional complications. Cessation of heparin will bring clotting to normal in a few hours. Dicumarol and Danilone have a more persistent

action. Even so, the use of Vitamin K. or Vitamin K. oxide will cut the waiting period.

The state of the myocardium must be improved in the presence of heart failure, auricular fibrillation, persistent tachycardia and rapid ectopic beats, with digitalis, Quinidine or Pronesthyl. The choice of the drug will depend on the urgency of the case at hand. Rapid digitalization with Digoxin, Cedilanid, or Ouabain might have to be undertaken in emergency. Anaemia should be treated with transfusion of whole blood or packed cells; hypoxia by early oxygen administration by face mask or nasal catheter. Hypotension should be treated with Levophed or Neosynephrine continuous intravenous drip, oxygen and blood transfusion. Dehydration and electrolyte imbalance should be treated by intravenous fluid and electrolyte therapy. Sedation should be accomplished with oral or rectal barbiturates, for example, Nembutal gr. ¾–1½. Moderate amounts of morphine, Demerol, Pantopon or codeine may be given in the presence of pain, although there are those who would refrain from giving opiates. In the presence of tachycardia, belladonna drugs may be omitted.

Case 3

Mr. J.P.S. (age, 63; weight, 202 lb.), entered the hospital for the repair of a ventral hernia. On admission, the patient was found to be suffering from the congestive heart failure. The admission summary states that he was dyspnoeic, cyanosed and coughing; his heart was enlarged and a rapid fibrillation was present; blood pressure was 150/110 and the pulse rate over 100/min.; basal rales were heard bilaterally. Because of the patient's obesity and varicose veins, it was not certain if he had distended neck veins or ankle oedema. Fluoroscopy showed the enlargement of the left auricle and ventricle; the EKG confirmed auricular fibrillation and myocardial ischaemia. The patient was put on the usual regimen for treatment of congestive heart failure which included low calorie and low salt diet and digitalization. When seen two weeks later at pre-anaesthetic rounds, he was free from dyspnoea at rest and also free from cough; he was fibrillating but at a much slower apical rate, and he was moving freely about the room. He had lost 12 pounds. The following morning, after Nembutal gr. 1½ rectally and morphine gr. ¼ s.c. premedication, this patient underwent an uneventful operation for his hernia under continuous segmental spinal anaesthesia.

Almost everything associated with anaesthesia and surgery is of necessity detrimental to the patient suffering from heart disease. Every effort must be made to understand the problem and appreciate the steps taken by the surgeon and medical man in preparing the cardiac patient for operation. The patient's chance of surviving the operation will depend more upon this preparation than the actual technique of the anaesthesia employed (6).

The circulation on which the transportation of the oxygen to the tissues and the metabolites from the tissues to the lungs depends may be impaired at the heart level as described in the preceding section, and then our attention will be concentrated on that organ. Very often, however, our concern is aroused by the knowledge of deleterious effects of reduced circulatory volume of blood or of its fractions.

We know that stagnant anoxia and anaemic anoxia are by far the greatest hazards in surgery and its prevention is of prime importance to the anaesthetist and surgeon alike. We also know that the patient's immediate postoperative and

subsequent recuperative periods will be influenced by the kind of attention given his circulatory deficits before the operation.

An estimation of the degree of the deficit present is a part of safe pre-anaesthetic planning. One has to be guided, of course, by the urgency of the case at hand, but, to use Bland's words, the policy of hurrying slowly will frequently have a beneficial effect on the subsequent mortality and morbidity. The occasions when the need for rapid preoperative preparations must be set above other considerations are relatively few. Usually we have more than enough time for proper evaluation and repair of the existing deficits. For one reason or another that precious time may be wasted, either through lack of appreciation of the possibility of deficit in the volume of blood or often through more hopeful than factual interpretation of the clinical and laboratory findings. It sounds superfluous to say that data giving the concentrations of haemoglobin, serum proteins or R.B.C. per 100 cc. of fluid may be misleading and may give a false sense of security. Yet, generally speaking, these are still the only data available in most of the cases. This "routine" kind of evaluation of the patient's circulatory powers throws little light on the actual volume of the blood, proteins or R.B.C. mass present. Clark *et al.* (7) have shown the existence of reduced blood volume, total haemoglobin and total R.B.C. mass in malignant disease, chronic infections, peptic ulceration, hepatic disease and malnutrition commonly seen in elderly people, commensurate with the weight loss. These losses were as follows:

Blood volume	67–79% of standard value = 85 ml./kg.
Average total haemoglobin	50–66% of standard value = 12.7 gm./kg.
Average total R.B.C. mass	56–70% of standard value = 40 ml./kg.

These results, checked by Evans blue dye blood volume studies, were in agreement with the relationship existing between the body weight and the blood volume postulated by the authors; a relationship strong enough to permit the prediction of existing blood volume deficit on the basis of weight loss alone, without taking into account sex, age and body surface area.

The authors suggest that when taking information on weight loss from the patient, the optimal weight in health should be inquired for and taken as one point of reference. They also feel that extremely obese, very tall and thin subjects, should have their blood volume deficit estimated on the basis of standard values for sex, age and body surface area rather than weight alone. They also point out that in gastro-intestinal bleeders, the values obtained tend to fall short of the actual loss sustained.

Case 4

E.C.S. (age, 64; weight, 134 lb.), was admitted for gastrectomy following the diagnosis of carcinoma of the stomach. His weight represented a loss of approximately 46 lb. since his best weight one year previously was 180 lb. Taking into consideration the weight loss alone, this man was short of about 1,700 ml. of blood. The total blood volume estimation using Evans blue dye technique revealed no deficit to be present. This finding could be correlated with the clinical appearance of the patient. Tall and of a large frame, he preserved his musculature quite well, despite weight loss. It could

be visualized that any wasting that had taken place occurred in body fat rather than the body muscle. The patient's physical power was little impaired and he carried his duties uninterrupted until his hospitalization.

To be on the safe side, the patient was given a transfusion of 500 ml. of whole blood before and 500 ml. during the operation, the latter to cover the operative blood loss. He withstood the four-hour operation very well and made a speedy recovery.

As their next logical step, Clark *et al.* (7) undertook the quantitative replacement of blood volume deficit by whole blood transfusions before major operations and thus, they feel, they increased the tolerance of otherwise "poor risk" patients. There has been no evidence of untoward effects of overfilling the vascular space, and no complications have been attributed to mild haemoconcentrations.

J. P. Crehan (8) in an article on blood volume replacement in poor risk patients, writes: "In smaller institutions, where elaborate blood volume studies are not practical or available, this method of evaluating blood volume deficiency in surgical patients, on the basis of the weight lost, is more satisfactory than no method at all."

Risking repetition, one should like to remind that time is necessary for transfusing, sometimes large quantities of blood, into depleted patients. This calls for early planning of replacement by all concerned with the operative welfare of the patient.

There seems to be a little disagreement as to the necessity of restoring the circulating blood volume following acute haemorrhage. Most people also feel that blood is the best fluid to replace blood lost. This may not always be possible but should always be strived for. This is adhered to not only because it seems so logical, but also because it stays in the circulation owing to the presence of the red cells in the fluid. Red cells also make blood a preferable agent for transfusion because of their oxygen and carbon dioxide carrying capacity through the medium of haemoglobin and because of the latter's function as an important buffer system.

Attempts have been made to establish a method for accurate assessment of acute internal or external blood loss. The usual criteria—blood pressure, pulse rate, pallor, coldness—are often masked in cases of compensated oligaemia. We know that latent shock may become apparent soon after induction of the anaesthesia, or when surgical interference or additional haemorrhage become superimposed.

It is seldom that we can see the actual amount of blood lost in an accident. Therefore, any ready-to-use yardstick or rule of thumb, although not exactly "scientific," is of help when one attempts to measure the amount of blood lost. Clark and Fisher of Birmingham Accident Hospital, in their recently published monograph (9) attempt to correlate blood loss with the size of the wound or the size of the swelling suspected to have been caused by haemorrhage. The authors have suggested that the flat of the hand or the size of the fist be used as yardsticks. Thus, a wound the size of the flat of one hand corresponds to approximately 500 cc. of blood; and a swelling the size of one first corresponds to an equal loss of blood. To support haemodynamics and to prevent shock in severely injured patients we now have several measures at our disposal: (*a*) blood, plasma, or plasma expanders to increase volume; (*b*) vasopressors to de-

crease vascular lumen; (*c*) short-term, quickly acting corticoids, such as soluble Hydrocortisone (Solu-cortef) for intravenous or intramuscular use; chlorpromazine (Largactil) and similar autonomic blocking drugs protecting organism against deleterious reflexes.

Case 5

Mr. C.V.D.H. (age, 18; weight, 150 lb.) was thrown out of the truck in which he was riding and sustained a severe injury to his abdomen. He was admitted in shock, his blood pressure was non-recordable and most of his bowel outside the abdominal cavity. There was a segment of small bowel and a portion of the anterior abdominal wall missing altogether. In addition, he had fractured several ribs and a clavicle. Subcutaneous emphysema was present.

As first aid measures, the patient was given 1000 ml. of plasma; morphine gr. ¼ intravenously; and oxygen through a nasal catheter. He responded well to this treatment. When seen preoperatively, his blood pressure was 90/60; pulse 120/min., weak; respiration 30/min. He was conscious and slightly restless. The respiratory movements of his chest were unequal, left side lagging behind the right. The intensity of the breath sounds on the affected side was diminished. There was at the time no displacement of the mediastinal structures.

Premedication consisted of Largactil 50 mg. and Demerol 50 mg. intramuscularly and atropine gr. 1/150 s.c. First available blood (500 ml.) was given immediately before induction of the anaesthetic. For maintenance, endotracheal N_2O/O_2 mixture (3/3 litre/min.), Demerol intravenously (total 175 mg.), Neosynephrine intravenous drip (1 mg. per 100 cc.) and an additional dose of Largactil (25 mg.) were used. During the operation which lasted 2¾ hours, most of the small bowel was resected and the rent in the anterior abdominal wall was successfully closed. The patient made a good, if stormy, recovery.

It is now well established that the adrenal-cortical steroids play an important role in adapting the organism to environmental changes and enable the patient to withstand stress brought about by the debilitating sickness, severe injury or overwhelming infections. This they do in a reciprocal relationship with the secretions of the adrenal medulla (epinephrine) and the pituitary (ACTH).

The function of the adrenal cortices may be suppressed by trauma (haemorrhage into the adrenals), acute infection (Waterhouse-Friderichsen syndrome) or chronic infection, usually tuberculosis (Addison's disease). However, in recent years, another factor has arisen and has grown in importance with the widespread use of cortisone preparations for the treatment of diverse disorders. This factor, it is felt, by suppressing the normal adreno-cortical activity is responsible for unexpected episodes of shock at the time of stress, such as an operative procedure. In the year 1952–3 there were several cases reported of fatal postoperative adrenal insufficiency involving patients who had received prolonged treatment with cortisone and who stopped taking cortisone before the operation. At necropsy, their adrenal cortices have been found to be atrophied.

Since that time several papers have been published on the subject, warning of the inherent danger and giving advice on the preventive steps to be taken when contemplating operation on these patients. No clear-cut answer could be found to such questions as to what dose of cortisone administered over what period of time is necessary to produce adrenal-cortical suppression. Lundy and Pender of The Mayo Clinic (10, 11) consider that there is danger for anyone who has received cortisone within three to six months before the proposed operation;

particular notice being given those who show symptoms of hyper cortinism (rounding of face, hypertension, peripheral oedema, hirsutism, pads of fat on the back of the neck). They seem to require special preparation unless they have had no cortisone for twelve months.

Any advice on how the extent of the adrenal-cortical depression may be determined before operation is tempered by mentioning that the tests available only measure separate functions of the adrenal cortex. There is no quantitative test to measure the amount of stress that the glands can cope with, and, of course, the stress imposed on an individual by various operations cannot be estimated.

Two tests are suggested as being both simple and available in all hospital laboratories (12). (*a*) In the Thorn Test (ACTH or eosinophil test) the adrenal cortex is stimulated, which is evidenced by a rapid fall in the circulating eosinophils. Failure to show a fall of 50 per cent or more, maximal in four hours, is considered to be a positive evidence of adrenal insufficiency.

(*b*) In the water-loading test insufficiency is shown by inability to produce a prompt diuresis after a rapid consumption of 20 ml./kg. of water.

Estimation of the urinary excretion of cortico-steroids and 17-keto-steroids, although reliable, can not be obtained in most general hospital laboratories. If the operation is an elective one, 200 mg. of cortisone (100 mg. in small children) should be administered intramuscularly 48, 24, and 1 to 2 hours before the operation. Prolonged fasting (late slating) and morphine are contraindicated. Premedication should be one-half of that prescribed normally for the same age and weight.

If the operation is to be performed as an emergency procedure, 200 mg. of cortisone should be administered intramuscularly and 100 mg. intravenously. More cortisone should be given intravenously during the operation if necessary.

The problem of adrenal insufficiency must then be faced in surgical patients who are known to suffer from chronic adrenal insufficiency, or who are suspected of having their cortices depressed by previous cortisone therapy. The presence of relative adreno-cortical insufficiency should also be suspected and the patient treated accordingly when shock develops without a readily demonstrable cause and the patient fails to respond to the usual resuscitative measures.

In such cases, cortisone should be administered intravenously as described above. For controlling hypotension, 4 mg. of norepinephrine (Levophed) or 5–10 mg. of Neosynephrine added to 1 litre of saline or 5 per cent glucose in saline solution should be administered. Plasma or plasma expander may be added to increase the circulating blood volume.

Case 6

Miss M.M. (age, 73; weight, 110 lb.), an elderly woman of rather frail constitution, had been hit by an automobile one afternoon and as a result suffered fracture of the forearm and ankle, the latter associated with much bruising and swelling of the leg. She was pale and in pain on admission, but not in shock. Her blood pressure was 130/90, pulse 60/min., respiration 20/min. Following medication, plaster of Paris casts were applied in order to immobilize the broken limbs, no attempt being made to reduce the fractures until the patient's general condition improved and the swelling subsided. The patient's general appearance did not improve, although she remained conscious and did not complain of pain. Several hours after the admission, the blood pressure steadily began to fall, but the pulse rate did not change. Then 500 ml. of whole blood was

started, but as no visible improvement occurred, the transfusion was combined with intravenous infusion of Neosynephrine 1 mg. per 100 cc. This raised the systolic blood pressure from 60 to 100 mm. Hg. However, the patient's blood pressure showed an immediate tendency to fall with slowing of the rate of the infusion, and she remained pale and apathetic. As the state of irreversible shock was feared to exist, 100 mg. of Solu-cortef was injected intravenously. This produced much improvement in the patient's appearance, her skin began to feel warmer, and blood pressure rose to 118/60 with Neosynephrine intravenous drip running at a very slow rate; the patient spent a comfortable night. In the morning, the Neosynephrine drip was discontinued, only 2 mg. of the drug having been used during the night, as against the 3.5 mg. used up in two hours preceding the administration of the cortisone.

A. W. Friend in his recent article on the subject of cortisone-induced adrenal suppression (12) draws attention to perhaps the most important aspect of this problem, namely, forehand knowledge of the possibility of such a state. He urges anaesthetists to be on the look-out for cortisone-treated patients who might have been taking cortisone preparations up to the last day before admission to hospital for elective surgical procedures. Sometimes, he points out, the information cannot be obtained from the patient. Then, he feels, it is the responsibility of the family doctor or anyone else prescribing cortisone drugs to provide the patient with a card clearly stating that that patient is or has been taking cortisone.

There is no reserve of fluid or electrolyte in the body which can be called upon when abnormal losses disturb the body balance. Imbalance in body fluid and electrolyte may occur as a result of shock, trauma, burns, gastric suction, vomiting, diarrhoea, and in such states as carcinomatosis, nephritis, diabetes and acute illness, such as pneumonia. In each case, losses are different in amount and nature.

The anaesthetist must make sure that his patient is in proper fluid and electrolyte balance before undertaking administration of the anaesthetic. This means that he must be on the alert for the existence of fluid and electrolyte imbalance, particularly in the very young and old. Further, he must be able to interpret clinical findings and data obtained from special tests.

The history should determine the amount and the type of fluid lost; the amount of fluid and food taken over the same period of time; whether thirst is present; and whether the patient has been perspiring a lot, has fever, feels weak, or is depressed.

The study of a patient's chart will enable the inquiring anaesthetist to sum up the amount of fluid lost and gained. Parenteral fluid is usually accurately measured, oral food can be estimated as fluid on the basis of approximately 70 per cent of its weight. Volumes of urine, gastric suction and vomiting are nearly always entered on the chart. To these must be added a rough estimate of the fluid passed from extensive burns, discharges and fistulae. There also must be added insensible obligatory losses (respiration, perspiration), which can be estimated on the basis of 0.7 cc. per kg. per hour when no fever is present and additional 0.1 per kg. per hour for each 2° F. of fever.

Simple water and sodium chloride depletion is the commonest, and hence the most important of the fluid and electrolyte problems seen clinically. In dehydration, the water loss is always associated with electrolyte loss and vice versa. The changes in intracellular electrolyte structure are always secondary to

initially untreated alteration in water and electrolyte in extracellular compartment.

In pure water depletion due, for example, to lack of intake for one reason or another, the extracellular fluid becomes hypertonic. In order to maintain isotonicity, water flows from the intracellular compartment into the extracellular. In other words, the dehydration occurs at the expense of the cells. As obligatory water losses through the skin and lungs continue unimpeded, and as kidneys working at their maximum concentrating power still require at least 500 ml. daily to excrete about 35 gm. of total solids, death would occur, under ideal conditions, on the seventh to tenth day of complete water deprivation.

Urinary output is reduced and urine is of high specific gravity; plasma sodium and chloride rise above normal; the blood urea is increased; the plasma volume remains unchanged until late. Thirst occurs early and persists; salivation decreases and dry mouth is a prominent symptom; there is progressive lassitude and hallucinations and delirium may occur. There is no postural fainting and there is no nausea, vomiting or cramps.

In the treatment of this type of dehydration, as in any other, prevention is most important. Those whose disease decreases their intake of water and food, or depresses the concentrating power of their kidneys, should have their water deficit made good by oral or intravenous administration of 5 per cent glucose in water. The administration of saline is contraindicated, as it would only add salt to already over-concentrated extracellular compartment. The guide to rational therapy is increasing urine volume, fall in blood urea and improvement in clinical appearance.

The sodium chloride balance is maintained by keeping intake above output and excretion of excess in the urine. Negative balance occurs owing to losses via the skin in sweat, by excessive gastro-intestinal discharges or inordinate loss in the urine in adrenal insufficiency. Simple restriction of sodium chloride intake only very slowly produces deficiency of any consequence, but a low intake in patients who are already suffering from losses by diarrhoea, vomiting, or Wangensteen suction, may become very important. In sodium chloride deficit, the kidney practically ceases to excrete the needed salt and conserves it much more readily than water. Sodium and chloride losses ultimately produce a fall in the osmotic pressure of extracellular compartment fluid, and with continuing renal water excretion, the extracellular compartment loses volume. If disorder is allowed to advance, in an attempt to maintain isotonicity between the two compartments, potassium may enter the extracellular fluid, whence it is promptly lost in the urine. The picture thus progresses from bad to worse and eventually any electrolyte abnormality is conceivable. If the amounts of sodium and chloride lost are isotonically not equivalent, acid-base balance will be altered.

Urinary volume remains unchanged providing an adequate water intake has been maintained; urine is of low specific gravity; urinary chlorides are absent; the blood volume is decreased and there is haemoconcentration; the blood urea is raised. In advanced cases of salt depletion, serum sodium, chloride and potassium are reduced and CO_2 combining power changed accordingly with the acid-base imbalance present.

Clinically, lassitude, orthostatic fainting and headache are early symptoms. There is no thirst, the skin becomes inelastic and feels dry; vomiting, nausea, and cramps are present; the blood pressure falls and eventually shock supervenes with cold clammy skin, pallor, narrow pulse pressure, stupor and coma.

If bowel atony, nausea and vomiting are absent, water and salt solutions can be given by mouth. If the intravenous route is to be used and if the condition is advanced, hypertonic saline, for example, 5 per cent sodium chloride is advisable. With the signs of clinical improvement, and with the reappearance of chloride in the urine this should be substituted with isotonic or hypotonic saline, for example, 500 ml. of 5 per cent glucose in water mixed with 500 ml. of normal saline. The use of hypotonic saline in geriatric patients is particularly recommended. The clinical picture, the serum sodium, the urinary volume and urinary chlorides are the best guides to treatment.

Relatively greater chloride than sodium deficit may result from loss of gastric secretions by vomiting, leading to alkali excess, that is, metabolic alkalosis. In such instances, sodium shifts to the intracellular compartment and potassium to the extracellular compartment, potassium being displaced by sodium excess. Again, potassium will be lost in the urine if water loss has not been too great, or if water alone is used for replacement therapy.

A solution containing relatively more chloride than sodium should be selected to which potassium has been added if alkalosis and further potassium chloride loss are to be prevented. Such solutions are Baxter's Travert 10%-Electrolyte No. 3., Darrow and Butler paediatric solution; or it can be made by adding 1 gm. of potassium chloride (13.4 mEq.) to 1 litre of normal saline.

Only rarely, in advanced alkalosis (for example, when cyanosis is present), ammonium chloride as 2 per cent solution will have to be given intravenously to provide excess of chloride ion. Potassium losses depend on other electrolyte and water changes. The deficiency of the ion may occur in alkalosis, as mentioned in the preceding paragraph, and in acidosis, for example, diabetic acidosis; in loss of intestinal and gastric secretions; in too vigorous administration of cortisone drugs or intravenous therapy of glucose and saline; in "stress" situations associated with anoxia and shock; in tissue destruction by trauma or disease, that is, with negative nitrogen balance.

Low serum potassium is always taken as evidence of depletion of intracellular potassium. Normal or high serum potassium levels, however, are not always representative of normal potassium level in the cells, because of the ionic shifts previously described.

Clinical symptoms and electrocardiographic changes are the result of the low serum potassium. Muscular weakness with diminished or absent reflexes is one of the earliest manifestations. Intestinal distension not responding to ordinary measures also occurs early. As the deficiency progresses, gasping respiration due to weakness of the respiratory muscles appears, together with the irregular pulse, increasing pulse pressure, venous distension and eventual heart failure from ventricular dilatation.

The electrocardiographic changes consist of prolongation of the Q-T interval, low wide T waves, and low voltage. Later the S-T segment becomes depressed

and "through" like, and T-wave is inverted. Premature beats appear and atrioventricular heart block follows.

As noted before, treatment of hypopotassaemia entails treatment of the total water and electrolyte imbalance. Potassium should be added in 13.4 mEq.–60 mEq. dose to repair solutions with 80 mEq./day as the maximum parenteral amount. The risk of producing dangerous hyperpotassaemia should be borne in mind, particularly in the presence of circulatory failure and renal insufficiency. Potassium is contraindicated in oliguria of whatever origin. The presence of potassium in transfused plasma and whole blood should not be overlooked, especially when banked blood or plasma are used.

The electrocardiogram, blood and urine studies and frequent clinical evaluation are the best guides to safe potassium therapy (13).

Conclusion

Evidence has been presented for the necessity of clinical evaluation of patients, far ahead of planned anaesthetic and surgical interference. Recognition of particular problem should be followed by appropriate preparation of the patient, the anaesthetist taking active interest in that preparation.

Résumé

En anesthésie, aujourd'hui, les troubles cardio-pulmonaires et circulatoires consécutifs à la maladie ou aux blessures deviennent les problèmes les plus fréquents. L'apparition de nouveaux médicaments pouvant influencer l'homéostasie tout en nous procurant des armes nouvelles n'a pas été sans faire naître également de nouveaux dangers.

Le médecin anesthésiste doit reconnaître le caractère et l'importance du trouble dans les systèmes vitaux de l'organisme. Pour atteindre ce but, il lui faut faire un examen physique complet et s'aider de certaines épreuves faciles qui peuvent être faites dans tous les hôpitaux ordinaires.

En plusieurs occurrences, il est nécessaire de prendre du temps pour préparer adéquatement un malade, qu'il s'agisse de transfusions à donner, d'équilibre hydrique ou électrolytique à rétablir, de drainage des voies respiratoires ou de digitalinisation. Il est du ressort de l'anesthésiste de surveiller que l'institution de ces traitements ne soit pas retardée jusqu'à la veille de l'opération. Il s'impose également qu'il comprenne ces traitements et devienne familier avec eux pour en continuer l'application le jour de l'opération.

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LETTERS TO THE EDITOR

2004, 7th Avenue South
Lethbridge, Alta.
October 7, 1957

The Editor
Canadian Anaesthetists' Society Journal
170 St. George St.
Toronto, 5

DEAR SIR:

Drs. Dobkin and Wyant reporting in the July number of your JOURNAL on the results of experiments on eight volunteers with intravenous anaesthetics state: "Hexobarbital. The mean period of apnoea with this drug was seven seconds with the same mean dose of 517 mg./M^2. There was virtually no depression of the respiration or the metabolic rate." They go on to say: "On the whole, hexobarbital had far less effect on either respiration or haemodynamics than thiamylal for the corresponding state." And later on they write: "All the drugs significantly depressed oxygen consumption except hexobarbital"; and finally: "Venous pressure was also reduced by all drugs by at least 15 per cent with the least changes observed with hexobarbital and buthalitone."

These observations all tend to confirm my own opinion (1) and to mention a few others, Morley, Blair Gould and Mushin (2,3,4,5), however, Drs. Wyant, Dobkin and Aasheim writing in the *British Journal of Anaesthesia* two months earlier (May, 1957) about five of these seven experiments with hexobarbital published in your JOURNAL state: "Because of its more detrimental effects, especially on respiration, hexobarbitone cannot be recommended."

These two publications by the same authors about the same experiments are difficult to assess unless "hexobarbitone" is a misprint for some other drug. If not it would be interesting to know what the changes in the last two experiments were that were of such magnitude that they altered the conclusions drawn from the previous five?

Yours truly,

J. SHEGOG RUDDELL, M.A., M.D., D.A., F.F.A.R.C.S.

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University of Saskatchewan
University Hospital
Saskatoon, Canada
October 23, 1957

The Editor
Canadian Anaesthetists' Society Journal
516 Medical Arts Building
Toronto 5, Ontario

SIR:

We want to thank you for sending us Dr. Ruddell's letter and allowing us to reply.

Dr. Ruddell objects to our statement in the *British Journal of Anaesthesia* (May, 1957) which seems to be contradictory to those made in this JOURNAL. Our graphs on pages 206 and 207 of the paper in the *British Journal of Anaesthesia* show very clearly that hexobarbital indeed compared favourably with the other agents studied as far as average tidal volumes and minute volumes are concerned. However, it should be noted that the wavy lines for hexobarbitone indicate marked irregularity of breathing patterns which causes difficulty in computing averages. If Dr. Ruddell will turn to page 198 of the same paper, he will read that there was crowing and periodic respiration, in addition to spontaneous often jerky, movements of the extremities. Thus on the whole, hexobarbital as an anaesthetic agent was inferior to both thiopental and thiamylal.

We must apologize for not having made this point clear, and probably our statement "especially on respiration" should have been more specific to avoid misunderstandings.

Yours faithfully,

GORDON M. WYANT, F.F.A.R.C.S.
ALLEN B. DOBKIN, M.D.

OBITUARIES

Leonard Sheldon Bartlett

It was with sincere regret that the Canadian Anaesthetists' Society learned of the sudden death of Dr. Bartlett on August 11, 1957.

Born in Ravenswood, Ontario, Dr. Bartlett had been a resident of Hamilton since 1942. Prior to coming to Hamilton he had been in general practice at Mount Elgin, Ontario.

After obtaining his B.A. degree at Western University, London, Ontario, he enrolled in Wesleyan Theological College in Montreal, Quebec, where he graduated with his B.D. He had a charge in Richlea, Saskatchewan, for several years before attending McGill University where he obtained his M.D., C.M.

degree. On coming to Hamilton, Dr. Bartlett became interested in anaesthesia and studied under Dr. Griffith of Montreal. He was taken on the Anaesthetic Staff of the Hamilton General Hospital in 1942. In 1951 he joined the staff of St. Joseph's Hospital on the Anaesthetic Service, where he remained an active member until his death.

In Hamilton, Dr. Bartlett was very well known in other fields besides medicine. He started the "Shut-Ins" Club which later grew to a large organization. This club was formed to bring entertainment to the old and infirm in hospitals and institutions in the form of movies, etc.

Dr. Bartlett was a former president of the Hamilton Angling and Hunting Association and for several years he was a director of the Huron and Erie Zone of the Ontario Federation of Anglers and Hunters. He was also chairman of the Wentworth Conservation Association and because of his medical background was well qualified to fight against the growing pollution of lakes and streams in his district.

Surviving, besides his wife, the former Albina Marie Quesnelle, are a son, Leonard Graeme at home, a daughter, Mrs. James Douglas Gardner (Margaret Patricia) of Hamilton, Ontario, his father, the Rev. Leonard Bartlett of Thamesville, two brothers, Dr. Oliver Russell Bartlett of Riverside, and Wallace Howard Bartlett of Toronto, and two sisters, Mrs. F. W. Haight of London, and Mrs. Geo. W. Sims of Chatham, Ontario.

Dr. Bartlett's funeral service was held at Barton Stone Church and he was buried in Barton Stone Church Cemetery, R.R. 4, Hamilton, Ontario.

William Easson Brown

Dr. William Easson Brown died suddenly at his summer home in Muskoka, August 30 on the last day of his summer vacation. Unknown to most of his friends he had had some warnings of possible future troubles, but his was the breed that would carry on life's usual functions without change and without regrets. In his last holiday he worked about his cottage even to the extent of activities involving some degree of manual labour. His was a busy life, too full possibly for his own good, with many interests apart from medical activities which he followed with intense zeal.

As a boy at high school (Harbord) and in his university period he was active in sports, particularly in track in which he was a keen competitor. He had an impressive record in the sprints in which he won many points for his teams. His interest in athletics in general and the University Track Club in particular was maintained unto the end. He never missed a meeting of the Track Club and for years he officiated at the inter-university track meets. He was a member of the Athletic Directorate of the University of Toronto for many years, a position he still held at the time of his death and one to which he devoted considerable time and thought.

Civilian flying was another of Dr. Brown's activities. Through the Toronto Flying Club he obtained his flying licence in 1929 and until recently he piloted

aeroplanes and seaplanes. He gave many of his friends a thrill and on occasion he flew a seaplane to his summer home. His association with the Flying Club gave rise to his appointment as Medical Examiner of flying personnel. He belonged also to the Aero Medical Society and the Civil Aviation Association.

Dr. Brown will be remembered longest for his research activities with reference to anaesthetic substances. While associated with the Department of Pharmacology and Professor Velyen Henderson he initiated studies with Ethylene, and with Professor George Lucas introduced the gas cyclopropane. Both are still widely used in the civilized world. As a clinical anaesthetist he was fearless in applying new techniques whether of his own invention or in investigation of methods reported in other centres. These sorties into new fields were always preceded by careful study or animal experimentation. He contributed a number of articles to various anaesthetic journals.

"Bill" as he was known generally to his friends was born the son of a doctor in Western Ontario. For a time the family lived in Chicago, eventually returning to Toronto where the boy grew up. From Harbord Collegiate in that city he entered Medicine at the University of Toronto, graduating M.B. in 1916. He served overseas as Captain in the C.A.M.C. at the Canadian Hospital at Orpington in England, in which hospital he began his anaesthetic career. On his return from his overseas duties he was appointed to the Anaesthetic Department of the Toronto General Hospital, a post retained until he reached the retiring age, at which time he was named consultant in Anaesthesia to the hospital. He was the recipient of many honours during his lifetime. He was granted the M.A. degree by his University for his thesis on Ethylene and Diploma of Anaesthesia by the conjoint board at the Royal College of Physicians and Surgeons (England) in 1938. He was a member of the Toronto Academy of Medicine, the Canadian Anaesthetists' Society, and the American Society of Anesthesiologists. He was a charter member of the Anaesthetic Travel Club,—now the Academy of Anesthesiologists. He belonged to the Aero Medical Society and was an Honorary Member of the Toronto Medical Legal Society. He was also an original member of the Caduceus Club, a Toronto Medical Dinner Society. From these activities he found time to act as Assistant Coroner for the City of Toronto. He was a cheerful soul with ever a joke or anecdote suitable for the occasion. His presence was felt in any company in which he found himself.

Our deepest sympathy goes to his wife, the former Irene Gallagher, and his three children, James Easson of Norbal, Ontario, Frederick Wallace at present in Casablanca, Morocco, and Patricia of Toronto. A third son, William, lost his life in the Second World War while serving as a gunner in the R.C.A.F.

H. J. SHIELDS

NEWS LETTER

Ontario

Ontario Division Meeting

The Ontario Division of the Canadian Anaesthetists' Society held a combined meeting with the Section on Anaesthesia of the Ontario Medical Association at the Royal Connaught Hotel in Hamilton on October 5, 1957. One hundred and fifty physicians were registered.

Guest speakers on the programme were Dr. James Elam of Buffalo, New York, who spoke on "Carbon Dioxide and Anaesthetic Apparatus"; Dr. Edmund Yendt of Toronto on "Citrate Poisoning in Rapid Transfusion"; and Dr. George Thomas of Pittsburgh, Pa., who demonstrated "Explosion Hazards in the Operating Room." In consideration of the widespread interest and multiple responsibility involved in the last subject, an invitation to attend was extended to the Ontario Hospital Association, and several operating room supervisors and hospital engineers attended. In addition, the following presentation by members of the Ontario Division completed the programme: "Adrenergic Blocking Agents in Shock," by Dr. Wolfgang Spoerel; "Meralgia Paraesthetica," by Dr. R. A. Chaplin; "Group Practice in Anaesthesia," by Dr. John D. Cameron; "The Evaluation of the Patient with Heart Disease for Anaesthesia," by Dr. H. B. F. Fairley.

A fine luncheon at St. Joseph's Hospital in Hamilton was combined with a question and answer period concerning the topics of the morning presentations. The day was concluded with a short business meeting followed by the "Sundown Hour (Cocktail Party)."

Eleven commercial exhibitors contributed greatly to the success of the meeting, and great interest was shown in the items which they displayed.

Dr. Helen Rossiter of London, Ontario, attended the Annual General Meeting of the Australian Society of Anaesthetists held in Adelaide in May, 1957.

Dr. Harry J. Shields of Toronto was elected President and Dr. Stanley M. Campbell Vice-President of the Academy of Anesthesiology at the meeting held in Reno, Nevada, in October, 1957.

Dr. C. W. P. Lunderville has been appointed Clinical Teacher in Anaesthesia at the University of Toronto. Dr. Lunderville is on the staff of the Department of Anaesthesia of the Toronto General Hospital.

Dr. B. G. Zielonka has been appointed to the staff of St. Joseph's Hospital, Toronto, in the Department of Anaesthesia.

Surgeon-Commander J. W. Green, R.C.N., is attached for postgraduate training to the Department of Anaesthesia, University of Toronto.

New Brunswick

Dr. David Power of St. Mary's Hospital, Montreal, gave two papers at the meeting of the New Brunswick Division held during the Annual Meeting of the

New Brunswick Medical at St. Andrews, August 25–28. His paper on the "Non-Surgical Dictates of Anaesthesia," given before the New Brunswick Medical group was well received by all present.

During the clinical session of the New Brunswick Division, Dr. Power and several of our members had an informal round table dealing with Dr. Power's paper on "The Anaesthetic Problems of Pelvic Eventration," and several other subjects.

A Clinical Meeting was planned for February, 1958, to be put on by the Moncton Group.

Meetings and Postgraduate Courses

Western Regional Meeting, Canadian Anaesthetists' Society, Calgary, Alberta, March 13–15, 1958

New Brunswick Division, Canadian Anaesthetists' Society, Clinical Meeting, Moncton Hospital, Moncton, N.B., February 15–16, 1958

Council, Canadian Anaesthetists' Society, Park Plaza Hotel, Toronto, March 1–2, 1958

Canadian Anaesthetists' Society, Annual Meeting, Seigniory Club, Montebello, Quebec, June 23–25, 1958

University of Kansas, Postgraduate Course in Anesthesiology, April 14, 15, 16, 1958

World Congress of Anaesthesiologists and Assembly of the World Federation of Societies of Anaesthesiologists, Toronto, Ontario, September 4–10, 1960

The third National Meeting of the Spanish Association of Anaesthesiology was held in Madrid on September 24–26, 1957.

The Canadian Anaesthetists' Mutual Accumulating Fund

The Mutual Accumulating Fund has been incorporated under the laws of Canada as instructed by the Annual Meeting of the Canadian Anaesthetists' Society on June 25, 1957. Application for registration of the Corporation as a Security Issuer has been made in each province, and shares will be available in each province as registration becomes effective. These shares are not available to residents of the United States of America.

REGIONAL BLOCK: A HAND BOOK FOR USE IN THE CLINICAL PRACTICE OF MEDICINE AND SURGERY. By DANIEL C. MOORE, M.D. Second edition. Springfield, Ill.: Charles C. Thomas; Toronto: The Ryerson Press. $11.00.

Once again Dr. Moore has presented a treatise on regional anaesthesia which is concise, clear, practical and illustrative. The author states that this book is not intended to be a reference book, but rather a handbook, and therefore references are not included.

Because the book is primarily for beginners, the author describes only those blocks that are used in everyday practice, omitting those used infrequently, those with a high incidence of serious complications, and those with residual paraesthesias.

The contents include a discussion of fundamental principles, indications for regional blocks, anatomy of the region, drugs available, materials used, technique, and complications that may occur. The work is so organized, that one may study any procedure without reading the entire book. Most of the nerve blocks in common use are discussed and described with excellent diagrams, photographs and drawings. When alternative procedures are available, the author describes only the one he prefers. He recommends persisting in one method to attain competence rather than attempting several approaches.

This book is valuable to the anaesthetist, surgeon, obstetrician, and general practitioner who may use regional anaesthesia.

D.C.

INTRODUCTION TO ANESTHESIA. By ROBERT D. DRIPPS, M.D., JAMES E. ECKENHOFF, M.D., and LEROY D. VANDAM, M.D. Philadelphia: W. B. Saunders Company. 1957. $4.75.

This 250-page volume presents anaesthesia in a practical fashion, the short chapters being in sections entitled "The Preanaesthetic Period," "The Day of Anaesthesia," "During Operation," "The Post-Operative Period" and "Special Topics." In the first two sections particularly, mention is made of using useful facts learned usually by experience but seldom recorded. The meticulous detail should be appreciated by all readers for it reveals a wide knowledge of and respect for anaesthesia, with the desire to "pass on the lore" of the subject.

There is a number of charts and diagrams, some of which are not necessary to illustrate the text. The choice of references has been carefully limited. Adequate mention is made of the newer drugs encountered by the anaesthetist.

All students of anaesthesia will find this book interesting, both for the vast amount of information set down and the opinions expressed by the authors.

S.A.F.

APPOINTMENTS AVAILABLE FOR POSTGRADUATE TRAINING IN ANAESTHESIA IN CANADIAN HOSPITALS APPROVED BY THE ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA

THE following information is derived from a survey recently conducted by the Canadian Anaesthetists' Society, and is published as provided by the hospitals and university departments concerned. It will be noted that the titles designating appointments of various grades vary from hospital to hospital. Specifically, the term *Resident* in some centres indicates a senior house appointment, available only after considerable training in Anaesthesia, while in other centres and individual hospitals it is a term applied to all postgraduate interns-in-training. The terminology used in each case below is that in use by the hospital or university in question, and the exact nature of each appointment must be deduced by reference to the qualifications required for it.

NEWFOUNDLAND

GENERAL HOSPITAL, ST. JOHN'S

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Resident Anaesthetist	3	1 yr.	1—Jan. 1—Oct.	$3,600.00 less $660.00 if living in	Previous experience in Anaesthesia desirable but not essential

Basic science training. There are no facilities for teaching basic sciences. Presentation of papers and informal discussions occur at regular departmental meetings.

Address applications to: Dr. E. Wilson,
Superintendent, General Hospital,
St. John's, Newfoundland.

NOVA SCOTIA

DALHOUSIE UNIVERSITY, HALIFAX

Teaching hospitals: VICTORIA GENERAL HOSPITAL
CHILDREN'S HOSPITAL
CAMP HILL HOSPITAL (D.V.A.)

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	3	1 yr.	0	$100.00/mo.	Graduate of Class A Medical School plus one year general internship
Resident Anaesthetist	3	1 yr.	2	$125.00/mo.	Residents are reappointed yearly for three years
Senior Resident	1	1 yr.	1	$150.00/mo.	

Basic science training. One year in Medicine or Basic Sciences available. Anatomy—one afternoon per week for six months; Pharmacology—two residents as demonstrators in the department; lectures by physiologist and members of the department of Anaesthesia. Residents are asked to attend suitable meetings of other services in the hospital and lectures given by outstanding visiting doctors to numerous refresher courses. Residents and interns are rotated through the Children's Hospital, the D.V.A. Hospital for periods of two to three months and to the Naval Hospital on a daily basis.

Address applications to: Dr. Carl Stoddard,
Victoria General Hospital,
Halifax, Nova Scotia.

NEW BRUNSWICK

SAINT JOHN GENERAL HOSPITAL

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	1	1 yr.	1	$75.00/mo. plus $25.00 living out allowance	Graduate of one year

Basic science training. Clinical teaching only.

Address applications to: Dr. Carl R. Trask,
Director,
Saint John General Hospital,
Saint John, New Brunswick.

QUEBEC

LAVAL UNIVERSITY, QUEBEC

Teaching hospitals: HÔTEL-DIEU DE QUÉBEC
LAVAL HOSPITAL, STE FOY, QUÉBEC

Hôtel-Dieu de Québec

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	0	1 yr.	0	$100.00/mo.	
Resident Anaesthetist	7	3 yrs.	0	$200.00/mo to $400.00/mo.	
Research Fellow	0	—	1	—	

Basic science training. Not specified. Senior interns spend the year in Medicine & Surgery.

Address applications to: Dr. Fernando Hudon,
Hôtel-Dieu Hospital,
Quebec, P.Q.

Laval Hospital, Ste Foy

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Resident Anaesthetist	2	1 yr.	2	$3,000.00 per annum	Two years training (minimum)

Basic science training. As provided by Laval University.

Address applications to: Dr. A. L'Espérance,
Medical Director,
Laval Hospital,
Ste Foy, Quebec

HÔPITAL DE L'ENFANT-JÉSUS, QUEBEC

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	1	1 yr.	1	$100.00/mo.	One year rotating internship, one year senior internship
Resident Anaesthetist	4	3 yrs.	1	$100.00/mo. to $300.00/mo.	
Clinical Assistant	3	—	0	—	Residency of three years

Basic science training. Weekly theoretical courses and instructions from staff members each morning. Teaching is in French.

Address applications to: Dr. Eugene Allard,
Chief, Department of Anaesthesia,
Hôpital de l'Enfant-Jésus,
Quebec, P.Q.

HÔPITAL ST. FRANCIS D'ASSISE, QUEBEC

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	2	4 mo.	1	$75.00/mo.	
Resident Anaesthetist	2	3 yrs.	2	$200.00/mo.	
Clinical Assistant	1	3 yrs.	1	$500.00/mo.	
Part-time	2	Indefinite	0	$200.00/mo.	

Four years training is acceptable by the College of Physicians of Province of Quebec, one year by the Royal College of Physicians and Surgeons of Canada.

Basic science training. Four hours each week of basic training from September to June.

Address applications to: Dr. Roland Duchesne,
Director of Anaesthesia,
Hôpital St. Francis D'Assise,
Quebec, P.Q.

HÔPITAL GÉNÉRAL ST. VINCENT DE PAUL, SHERBROOKE

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Resident Anaesthetist	1	1 yr.	1	$125.00/mo.	Graduate of approved Medical School

Basic science training. Not specified.

Address applications to: Dr. Fernand Tanguay,
Medical Director,
Hôpital Général St. Vincent de Paul,
Sherbrooke, P.Q.

GENERAL HOSPITAL, VERDUN

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Resident Anaesthetist	1	1 yr.	1	$400.00/mo.	

Basic science training. Not specified.

Address applications to: Anaesthesia Service,
200 Church St.,
Verdun, P.Q.

McGILL UNIVERSITY, MONTREAL

Teaching hospitals—MONTREAL GENERAL HOSPITAL
ROYAL VICTORIA HOSPITAL, MONTREAL
MONTREAL NEUROLOGICAL INSTITUTE
CHILDREN'S MEMORIAL HOSPITAL, MONTREAL
ST. MARY'S HOSPITAL, MONTREAL
QUEEN MARY VETERAN'S HOSPITAL, MONTREAL
QUEEN ELIZABETH HOSPITAL, MONTREAL
REDDY MEMORIAL HOSPITAL, MONTREAL
ROYAL EDWARD LAURENTIAN HOSPITAL, MONTREAL

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Resident in Anaesthesia	36	3 yrs.	Some July 1	1st yr. $100.00/mo. 2nd yr. $150.00/mo. 3rd yr. $150.00/mo. plus either an allowance or full maintenance	Rotating internship

The course is three years, leading to a Diploma in Anaesthesia from McGill University. Students are assigned for clinical residency to the co-operating hospitals on a six-month rotation basis.

Basic science training. Organized courses in Anatomy, Physiology, Biochemistry, and Pharmacology are conducted by the various university departments. Two-hour seminars are held two evening a week throughout the teaching session of thirty weeks.

Research. The Wellcome Foundation Anaesthesia Research Department of McGill which is under the direction of Professor Gordon Robson enables postgraduate students to study methods of research in Anaesthesia. Those postgraduate students specially interested in learning or undertaking projects in this field may write to Professor Gordon Robson direct.

For short-term residency in the above hospitals apply directly to the Head of the Department of Anaesthesia of that particular hospital.

Fees payable to: McGill University
Basic Science Course—$155.00
Annual Registration Fee—$10.00.

Address applications to: R. G. B. Gilbert, M.B.,
Chairman of the Department of Anaesthesia,
McGill University,
Montreal Neurological Institute,
Montreal 2, P.Q.

Montreal Children's Hospital and Reddy Memorial Hospital, Montreal

Senior residency appointments are available for up to two years' recognized training, predominantly paediatric. The majority of the junior resident staff are obtained as part of the McGill diploma training program. However, independent inquiries are welcome, and those interested in obtaining special experience in paediatrics can usually be catered for if they will apply directly to:

Dr. H. T. Davenport,
Director of Anaesthesia,
Montreal Children's Hospital,
2300 Tupper St.,
Montreal, P. Q.

Royal Victoria Hospital, Montreal

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Assistant Residents	5	6—12 mo.	5	$100.00/mo. plus $40.00/mo. living out allowance	Approved junior rotating internship
Assistant Residents	4	6—12 mo.	4	$150.00/mo. plus $40.00/mo. living out allowance	One year postgraduate training in anaesthesia
Resident in Anaesthesia	3	6—12 mo.	3	$200.00/mo. plus $40.00/mo. living out allowance	Two years post-graduate training in anaesthesia
Clinical Fellow	4	1 yr.	2—Jan. 1 2—July	$600.00/mo.	These appointments available to students of the final year of supervised practice, required by the R.C.P.S. of Canada for Certification

Basic science training. As a participating hospital in the McGill Diploma Course in Anaesthesia, all members of the resident staff are encouraged to register as postgraduate students at McGill.

Address applications for resident appointments to: Dr. J. Gilbert Turner,
Executive Director,
Royal Victoria Hospital,
Montreal 2, P.Q.

Address applications for Clinical Fellowships to: Dr. A. B. Noble,
Anaesthetist-in-Chief,
Royal Victoria Hospital,
Montreal 2, P.Q.

UNIVERSITY OF MONTREAL, MONTREAL

Teaching hospitals: HÔPITAL MAISONNEUVE,
HÔPITAL NOTRE-DAME,
HÔTEL-DIEU DE MONTRÉAL

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	10		12	$90.00/mo.	
Resident Anaesthetist	10		12	$250.00/mo.	
Clinical Assistant	5		10	$300.00/mo.	

Basic science training: Pharmacology—12 lectures; Biochemistry—12 lectures; Anatomy—12 lectures; Physiology—12 lectures; and clinical application in different hospitals.

Address applications to: Dr. Léon Longtin,
University of Montreal,
Montreal, P.Q.

Maisonneuve Hospital (& Institute of Cardiology)

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	1	1 yr.	1	$200.00 to $250.00/mo.	One year rotating internship
Resident Anaesthetist	2	1 yr.	2	$300.00 to $350.00/mo.	Rotation plus one year senior internship in Anaesthesia
Clinical Assistant	4	1 yr.	3	$400.00 to $450.00/mo.	Two years' training in Anaesthesia
Clinical Fellow	3	6 mo. plus	1	$500.00/mo. up	Three years' training in Anaesthesia (pending certification or newly certified)

Basic science training. As provided by Diploma Course at University of Montreal or McGill University.

Address applications to: Dr. Marius Dubeau, Director, Department of Anaesthesiology,
Maisonneuve Hospital,
5415 L'Assomption Blvd.,
Montreal 36, P.Q.

ONTARIO

UNIVERSITY OF TORONTO, TORONTO

Teaching hospitals: TORONTO GENERAL HOSPITAL
TORONTO WESTERN HOSPITAL
ST. MICHAEL'S HOSPITAL, TORONTO
HOSPITAL FOR SICK CHILDREN, TORONTO
TORONTO EAST GENERAL AND ORTHOPAEDIC HOSPITAL
WOMEN'S COLLEGE HOSPITAL, TORONTO
SUNNYBROOK HOSPITAL (D.V.A.), TORONTO
NEW MOUNT SINAI HOSPITAL, TORONTO
HAMILTON GENERAL HOSPITAL, HAMILTON

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	21	2 yrs.	10	$1,000.00 to $1,400.00	(1) Qualification registrable to practise medicine in Ontario (2) One year rotating internship
Resident Anaesthetist	5	1 yr.	5	$1,800.00 plus $300.00 from University	As above plus two years' training in Anaesthesia
Clinical Assistant	2	1 yr.	1	—	As for Resident Anaesthetist plus one year in Internal Medicine or a Basic Science
Research Fellow	2	1 yr.	1	$2,000.00	As for Resident Anaesthetist plus some experience in research in a basic science

Basic science training. Anatomy—32 one and a half hour lecture demonstrations in Department of Anatomy; Pathology—lecture of one and a half hour a week for eight months a year; Physiology—lectures and seminars during two-year period from Sept. to May; Pharmacology—lectures and seminars during two-year period from Sept. to May.

Address applications to: Dr. S. M. Campbell, Associate Professor,
Department of Anaesthesia,
University of Toronto

ST. JOSEPH'S HOSPITAL, TORONTO

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	1	1 yr.	0	$1,700.00	1 yr. rotation 1 yr. anaesthesia
Resident Anaesthetist	1	1 yr.	0	$3,000.00	2 yrs. training in anaesthesia
Other (Junior)		1 mo.	1	$1,400.00	Graduate of recognized medical school

Basic science training. None.

Address applications to: Sister Superior,
St. Joseph's Hospital,
Toronto, Ontario

QUEEN'S UNIVERSITY, KINGSTON

Teaching hospitals: KINGSTON GENERAL HOSPITAL,
HÔTEL-DIEU HOSPITAL, KINGSTON

Kingston General Hospital

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	1	1 yr.	1	$200.00/mo.	Junior rotating internship
Resident Anaesthetist	1	1 yr.	1	$250.00/mo.	Junior rotating internship plus one year training in Anaesthesia

Basic science training. As arranged with individual university departments.

Address applications to: Dr. W. A. Campbell,
Chief, Department of Anaesthesia,
Kingston General Hospital,
Kingston, Ontario

Hôtel-Dieu Hospital

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	2	1 yr.	2	$200.00/mo.	One year rotating internship

Basic science training. Weekly seminars, covering physiology, pharmacology, anatomy and biochemistry and their application in Anaesthesia.

Address applications to: Dr. V. A. Nekus,
Department of Anaesthesia,
Hôtel-Dieu Hospital,
Kingston, Ontario

UNIVERSITY OF WESTERN ONTARIO, LONDON
Teaching hospitals: VICTORIA HOSPITAL, LONDON
ST. JOSEPH'S HOSPITAL, LONDON

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	1	2 yrs.	Jan. 1/58–Jan. 1/59	$150.00/mo.	Junior rotating internship plus L.M.C.C.
	2	2 yrs.	July 1/58–July 1/59	$125.00/mo.	
Resident Anaesthetist	1	1 yr.	Jan. 1/58–Jan. 1/59	$150.00/mo.	Two years as senior plus L.M.C.C.

Basic science training. Senior and Resident interns are required to spend part time at the Medical School as Research Assistants during their internships in addition to their hospital work. Grants are usually available from which additional remuneration is received.

Address applications to: Dr. J. A. Blezard,
Head of Department of Anaesthesia,
University of Western Ontario,
London, Ontario

Westminster Hospital (D.V.A.), London

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Assistant Resident	1	1 yr.	1	$2,700.00	Two years acceptable postgraduate training, not necessarily in Anaesthesia

Basic science training. Not specified.

Address applications to: Dr. William Bugg,
Assistant Medical Superintendent,
Westminster Hospital,
London, Ontario

OTTAWA CIVIC HOSPITAL

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Resident Anaesthetist	3	1 yr.	3	$200.00/mo. plus full maintenance	One year rotating internship

Basic science training. A series of basic science lectures, organized by the Post-Graduate Education Committee, and available to all interns.

Address applications to: Superintendent,
Ottawa Civic Hospital,
Ottawa, Ontario

HAMILTON GENERAL HOSPITAL, HAMILTON

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	2	1—6 mo. 1—3 mo.	1	$175.00/mo.	
Resident Anaesthetist	1		1—July		To be in final year of postgraduate course in Anaesthesia

One senior intern rotating three months on Anaesthesia, the other nine months through Paediatrics, Medicine and Obstetrics. At present one senior intern is provided from postgraduate course in Anaesthesia at University of Toronto for a period of six months rotation.

Basic science training. Not specified.

Address applications to: Medical Assistant to the Superintendent,
Hamilton General Hospital,
Hamilton, Ontario

ST. JOSEPH'S HOSPITAL, HAMILTON

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Resident Anaesthetist	1	1 yr.	1	$150.00 to $200.00/mo.	One year rotating internship plus L.M.C.C.

Basic science training. None. Training consists of instruction in inhalation, intravenous, spinal, regional and rectal anaesthetic techniques. Weekly review of literature presented to staff, and bi-annually to section of Anaesthesia of Academy of Medicine.

Address applications to: Dr. Karl Kraft,
Director of Anaesthesia,
St. Joseph's Hospital,
Hamilton, Ontario

MANITOBA

ST. BONIFACE HOSPITAL, ST. BONIFACE

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	2	1 yr.	2	$225.00/mo.	Graduate from Grade A Medical School plus one year rotating internship
Resident Anaesthetist	2	1 yr.	0	$350.00/mo.	As above plus one year senior intern in Anaesthesia
Clinical Assistant	1	1 yr.	0		
Clinical Fellow	1	1 yr.	0		

Basic science training. Yearly course of lectures by the Manitoba Medical College. The course includes lectures in Anatomy, Physiology, Biochemistry and Pharmacology.

Address applications to: Dr. M. Minuck,
St. Boniface Hospital,
St. Boniface, Manitoba

DEER LODGE HOSPITAL (D.V.A.), WINNIPEG

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	1	2 yrs.	0	$250.00/mo.	One year rotating internship

Basic science training. Weekly lectures in Basic Sciences in conjunction with the University of Manitoba postgraduate course.

Address applications to: Director of Department of Anaesthesia,
Deer Lodge Hospital,
Winnipeg 12, Manitoba

WINNIPEG GENERAL HOSPITAL, WINNIPEG

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	2	1 yr.	0	$900.00 plus board and room	
Assistant Resident	1	1 yr.	1	$1,500.00 to $1,800.00	
Resident Anaesthetist	1	1 yr.	1	$2,100.00 to $2,700.00 plus board and room	
Clinical Assistant	1	1 yr.	1	$4,000.00	

Basic science training. Training is provided through the Basic Science Departments of the University of Manitoba.

Address applications to: Dr. D. M. Huggins, Department of Anaesthesia,
Winnipeg General Hospital,
Winnipeg, Manitoba

SALVATION ARMY GRACE HOSPITAL, WINNIPEG

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Resident	1	6 mo.	1	$250.00/mo.	

Basic science training. University of Manitoba postgraduate training programme in Anaesthesia.

Address applications to: Dr. S. M. Luginsky,
Salvation Army Grace Hospital,
200 Arlington St., Winnipeg, Manitoba

CHILDREN'S HOSPITAL, WINNIPEG

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Clinical Assistant	1	1 yr.	1	Not more than $400.00 per mo.	2 yrs. "basic" training in Anaesthesia in a recognized hospital taken previously
Clinical Fellow	1	1 yr.			

Basic science training. Post-Graduate Course in Anaesthesia, University of Manitoba.

Address applications to: Dr. T. J. McCaughey,
Director, Dept. of Anaesthesia,
Children's Hospital,
Winnipeg, Manitoba

SASKATCHEWAN

UNIVERSITY OF SASKATCHEWAN, SASKATOON

Teaching hospitals: UNIVERSITY HOSPITAL, SASKATOON
SASKATOON SANATORIUM

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	2	1 yr.	2	$150.00/mo.	Rotating internship if practising in Canada, internship not required if alien returning home after training
Resident Anaesthetist	3	2 yrs.	3	$200.00/mo. to $225.00/mo.	Senior internship in Anaesthesia or Medicine
Research Fellow	1	1 yr. (renewable)	1(?)	$6,000.00/yr.	Full training; preferably holding higher qualification

Basic science training. A full range of seminars (3 per week) is provided covering all basic sciences as related to Anaesthesia. Some of these seminars are given by members of the Departments of Anatomy, Physiology, and Pharmacology. Test-papers are given from time to time as certain aspects of basic science fields are completed.

Address applications to: Dr. Gordon M. Wyant,
Professor of Anaesthesia,
University of Saskatchewan,
Saskatoon, Saskatchewan

REGINA GENERAL HOSPITAL, REGINA

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Resident Anaesthetist	2	1 yr.	1	$250.00/mo.	1 year rotating internship

Address applications to: The Superintendent,
Regina General Hospital,
Regina, Saskatchewan

ALBERTA

UNIVERSITY OF ALBERTA, EDMONTON

Teaching hospitals: UNIVERSITY HOSPITAL, EDMONTON
EDMONTON GENERAL HOSPITAL,
ROYAL ALEXANDRA HOSPITAL, EDMONTON

University Hospital, Edmonton

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	2	2 or 3 yrs.	1	$100.00/mo. to $125.00/mo.	One year rotating internship
Resident Anaesthetist	2	1 or 2 yrs.	1	$150.00/mo.	As above plus one year in Anaesthesia
Clinical Assistant	2	1 yr.	0	Variable on percentage	Eligible for certification
Research Fellow	2	1 yr.	2	$150.00/mo. to $200.00/mo.	One year rotating internship

Basic science training. Three hours weekly in Laboratory, Pharmacology and Physiology. Weekly lectures. Research six months to twelve months for Fellowship candidates in Physiology, Pharmacology, Cardiovascular or Pulmonary Laboratories.

Address applications to: Intern Committee,
University of Alberta Hospital,
Edmonton, Alberta

Edmonton General Hospital

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Resident Anaesthetist	1	1 yr.	1	$125.00/mo.	As required by Royal College of Physicians and Surgeons of Canada

Basic science training. Weekly seminars in conjunction with the Department of Anaesthesia, University of Alberta Hospital. Physiology and Pharmacology laboratory work can be arranged through the University of Alberta.

Address applications to: The Medical Director,
Edmonton General Hospital,
Edmonton, Alberta

CALGARY GENERAL HOSPITAL, CALGARY

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	2	1 yr.	0	$125.00/mo.	One year rotating internship

Basic science training. None.

Address applications to: Dr. Crosby Johnson,
Administrator,
Calgary General Hospital,
Calgary, Alberta

BRITISH COLUMBIA

UNIVERSITY OF BRITISH COLUMBIA, VANCOUVER

Teaching hospitals: VANCOUVER GENERAL HOSPITAL
SHAUGHNESSY VETERAN'S HOSPITAL (D.V.A.), VANCOUVER

Vancouver General Hospital

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Resident Anaesthetist	2		0	$230.00/mo.	
Associate Resident	5		0	$205.00/mo.	
Assistant Resident	6		0	$160.00/mo.	
Clinical Fellow	1		0	$300.00/mo.	
Research Fellow	1		0	$200.00/mo.	
Other	3		3	$205.00/mo.	

Basic science training. University of British Columbia, Basic Science Department.

Address applications to: Dr. H. B. Graves,
Director,
Department of Anaesthesiology,
Vancouver General Hospital,
Vancouver 9, British Columbia

Shaughnessy Veteran's Hospital, Vancouver

Appointments	Number	Duration	Available 1958	Remuneration	Requirements
Senior Intern	2	1 yr.	2	$175.00/mo.	One year junior internship
Resident Anaesthetist	1	1 yr.	1	$250.00/mo.	Six months to one year senior internship in Anaesthesia
Clinical Assistant (supervised practice)	1	1 yr.	1	$500.00/mo.	During or immediately following this position the incumbent becomes eligible for certification in Anaesthesia by examination

Basic science training. Weekly lectures of two hours during academic year at University of British Columbia.

Address applications to: The Superintendent,
Shaughnessy Hospital,
Vancouver 9, British Columbia

ST. PAUL'S HOSPITAL, VANCOUVER

Details not available.

Address applications to: Sister Superior,
St. Paul's Hospital,
1081 Burrard St.,
Vancouver 1, British Columbia

Anæsthesia

JOURNAL OF
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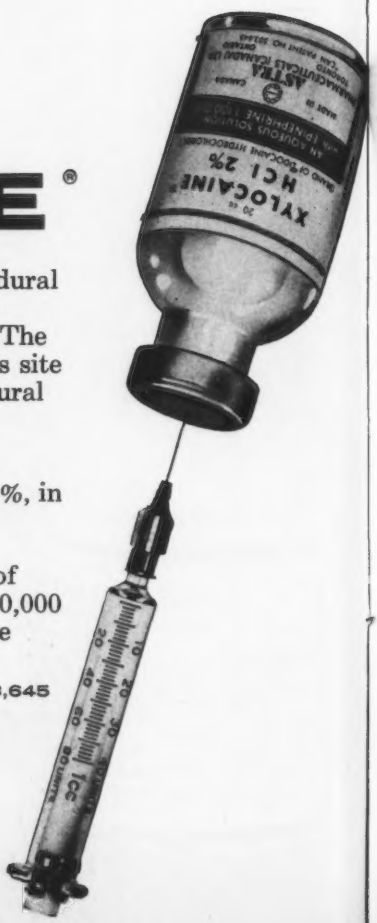

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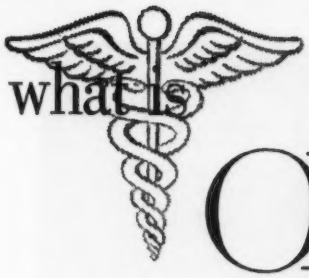

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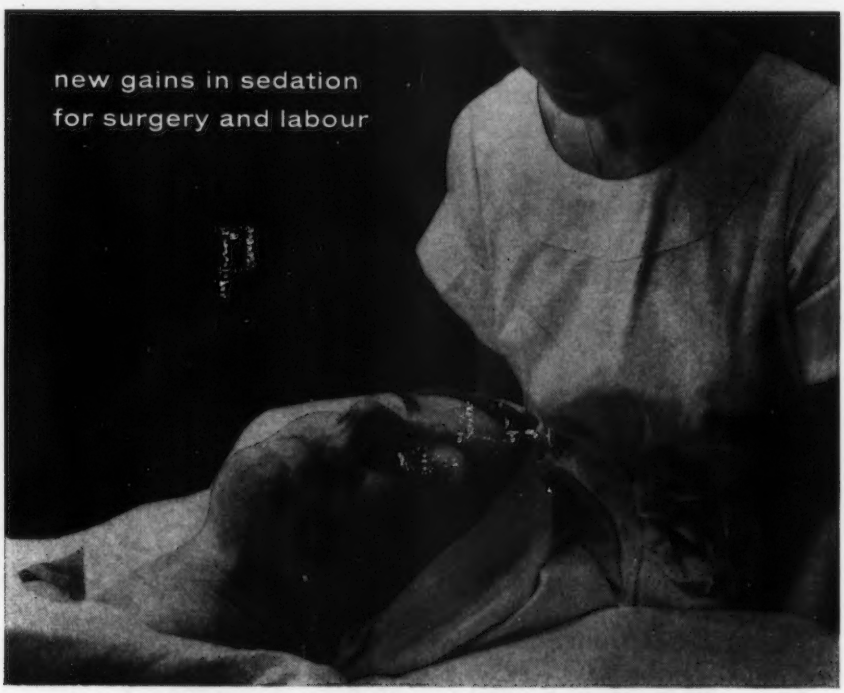

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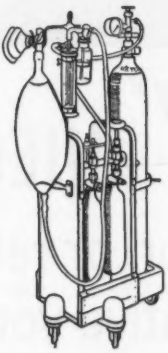

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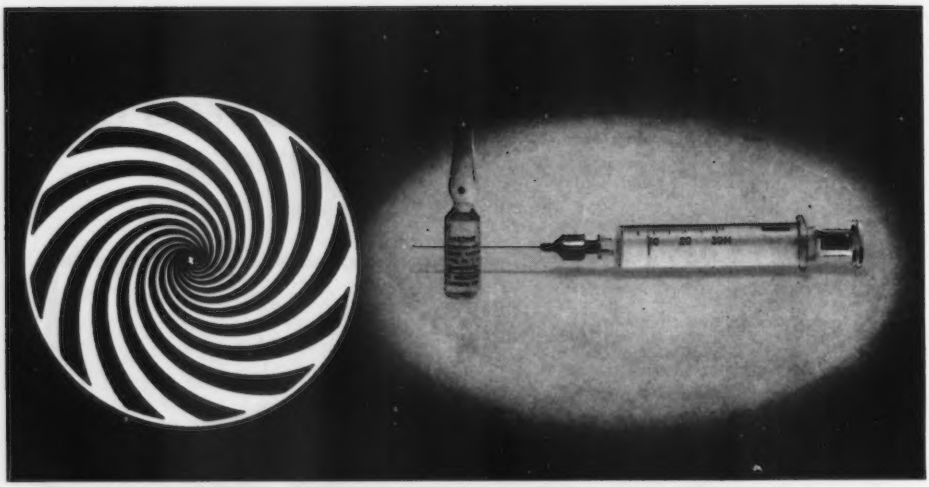

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1. Dent, S. J., Ramachandra, V., and Stephen, C. R.: Postoperative Vomiting: Incidence, Analysis and Therapeutic Measures in 3000 Patients, Anesthesiology. To be published. 2. Marcus, P. S., and Sheehan, J. C.: The Treatment of Postoperative Vomiting, Anesthesiology, *16*:423, 1955.

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4. Griffith, H. R. & Johnston, G. E. The Use of Curare in General Anaesthesia. Anesthesiology 3: 481 (1942).

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